ON THE RÔLE OF INSECTS, ARACHNIDS AND MYRIAPODS, AS CARRIERS IN THE SPREAD OF BACTERIAL AND PARASITIC DISEASES OF MAN AND ANIMALS. A CRITICAL AND HISTORICAL STUDY.

By GEORGE H. F. NUTTALL, M. D., Ph. D.,

Late Associate in Hygiene, Johns Hopkins University, Baltimore; Volunteer Assistant, Hygienic Institute, Berlin.

FROM THE JOHNS HOPKINS HOSPITAL REPORTS, VOL. VIII.

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(Plates I-III.)

Whilst hygienists have given much attention to the study of pathogenic organisms in air, water, soil and food, their behavior under different chemical and physical conditions, as also to the possibility of their direct or indirect transmission from diseased to healthy individuals; relatively little attention has been paid to one of the means by which infectious diseases are spread, to the rôle played especially by insects, which may serve either as carriers or intermediary hosts of disease-agents. The most thorough work in this direction has been done by parasitologists. Very few of the works on hygiene even mention the rôle of insects as carriers of infection, and those that do, generally speak vaguely on the subject.

The object of this publication is to present to the reader what is known, in the hope that the perusal of its contents will perhaps stimulate a few to undertake researches along these lines. The writer has been to considerable pains to gather what has been published, the various contributions being often difficult of access, and the literature exceedingly scattered. That flies may serve as carriers of pathogenic bacteria has long been claimed, but the amount of experimental work done to determine the accuracy of this frequently gratuitous assumption is exceedingly small. From the experience the writer has had in gathering the data here presented, he is fully aware of the fact that he may have overlooked some observations that are recorded in the literature. For this reason he will be grateful if his attention is drawn to any omissions, it being easy to add what has been left out at some future time. This

appears to be the first attempt made to gain a general view of the part played by insects, etc., in infectious diseases. The mention of diseases due to insects themselves, as well as those due to the agency of other small animals (crustacea, worms, mollusks, etc.) has been purposely omitted. It has also been deemed advisable not to include cases where complications, probably due to secondary bacterial invasion, have followed the bites or stings of venomous insects. The effects, which at times follow the bites of *Ixodidae*, *Trombidium* and *Sarcopsylla penetrans*, had to be considered, because it has been claimed by some authors that these may be capable of inoculating disease germs; it, however, only having been proved in the case of the cattle-tick that the latter is able to communicate Texas fever to healthy animals. The object of this communication is more especially to bring out the part played by these small animals in communicating infectious disease from sick to healthy subjects.

Anthrax and Flies.

After having read the rather extensive literature on the subject I have been struck by the very few positive cases recorded of anthrax arising from the bites of flies. Many authors present very positive opinions, but no evidence. In many cases the sharp pain which draws attention to the part affected, as well as the local appearances, have undoubtedly led to false statements. This was already stated by older authors, and a number of these in consequence go so far as to deny that malignant pustule may arise from the bite of a fly.

Bojanus[28] writes, "in such cases a small black spot appears, which is often (especially in those countries where man is often affected by anthrax and people are not able to form a clear judgment as to its origin) pronounced to be the sting of an insect." Larrey[14] (1824) says of the pustule: "The latter turns red, swells readily, and causes the patient to believe that he has been bitten by an insect or something of the kind;" . . . "we had twelve such cases in the Military Hospital at Toulon, almost all at the same time, in the middle of May. Frequent rains were followed by great heat. As these places are the first to become adorned with the verdure of spring, the soldiers and inhabitants go there by preference to take walks. All who were affected by a carbuncle said they had been bitten by an animal just after they had seated themselves on the fresh grass." Schröder[19] in Saxony wrote: "It is certainly true that some patients experience a sharp, penetrating sting, which they say they cannot compare with anything else but that of a severe insect bite, and that is

why, no doubt, they state that something has stung them; but if asked what has stung them they never know, saying they did not see the animal. It is true, as stated, that a sensation very much like that of an insect's bite occurs in a number of cases and first draws attention to the seat of the affection." Schwabe[21] (1838) states it as his experience, frequently repeated, that, "The patients, whilst feeling perfectly well, had for a moment the sensation corresponding to that of the bite of an insect at the spot where the pustule subsequently formed. They were in the open air at the time they felt the sting, and the part affected was always uncovered by clothing." Wendroth[22] (1838) cites a couple of cases such as Heusinger[39] (1850) had also experienced. The first is that of a woman who in the month of August, 1829, whilst harvesting, felt a sharp and evanescent pain on the breast, which she rubbed and scratched. On the way home that evening she felt unwell. On the fifth day she was dead. Heusinger (p. 451) remarks in this connection that these cases, occurring as they do almost entirely in districts affected by anthrax, probably are due to the burial thereabouts of animals dead of the disease. Haupt[24] (1845), writing of anthrax in Siberia, says the same thing, that persons feel a stinging sensation and unconsciously rub and scratch the place with the hand. Bollinger[44] (1874) writes that the subjective deception often leads the patient to say he has been bitten by a fly "whereas the infection occurred through direct contact." Joly[137] (1898) cites a case of a woman who claimed she had been bitten by a fly where the pustule developed, but when asked if she had seen the insect she said no. A similar case has come under my personal notice.

It is on such evidence as this that Schröder[19], Carganico[20] (1835) and Bongard[15] (1826) deny that the infection takes place through the agency of flies, and state that it usually comes from contact. Defays[35] (1868) also denies that flies cause anthrax. O. Finsch ("Reise nach West-Sibirien im Jahre, 1876," Berlin, 1879, p. 4331, to whose work my attention was drawn by my friend, Professor H. H. Behr of San Francisco), who witnessed the devastation caused by anthrax amongst the reindeer in Siberia, says he does not believe in the truth of the assertion that flies and gnats play a rôle in the spread of this disease. "For if these assertions were right," he writes, "not a living thing would be able to exist on the Tundra. Even ourselves, who lived continually exposed in an atmosphere which must have been filled by the spores of the *Bacillus anthracis*, who were bitten daily by hundreds of gnats, which attacked us immediately after leaving diseased reindeer, settling on us, and our suppurating gnat bites, must then have been hopelessly lost. That human beings die from eating the meat of reindeer affected by anthrax is now known by nearly everybody on the Tundra, which we are able to confirm as being a fact." He

describes how the healthy animals return to those that have died, snuffing about and licking their fallen companions. The air swarmed with gnats (*Culex pipiens*), from which Finsch and his companions suffered a great deal. Most authors, however, hold a contrary opinion:

Montfils[4] (1776) believed that anthrax might result from the bite of a fly. Matthy[9] (1801) thought that it might be due to some insect coming from India, and he cites cases where the patients supposed they had been bitten by flies. Chevalier[27] and Renault[26] cite cases where infection was attributed to insect-bites. Thomassin[6] (1780) thought that the bites of different insects caused anthrax. Wagner[1], Enaux and Chaussier[7] (1785), Mellado[11] (1815), Ziegler[13] (1822), Regnier[17] (1829), Herbst[12] (1822), and Gilbert[8] (1797) believed that insects gave rise to anthrax by their bites. Wagner, Glaser[5] (1780), Hasenest and Hintermayer[25] (1846) blame wasps as well as biting flies. Mellado[11] (1815) describes 11 cases of malignant pustule in man where he believed no contact with infected animals or meat had taken place. He thought infection came through insect-bites. It is needless to dwell on the "*Furia infernalis*" of Linnæus (1827), an imaginary fly which was supposed to attack and cause the death of the reindeer in Lapland. Joseph[55] states that Pallas, as well as Gebler (1827), attributed the Siberian carbuncular disease to the agency of flies or their bites, and Fischer (1818-1830) thought the same with regard to a similar affection which was observed in Thuringia, though of the many thousands attacked none ever saw the insect that was supposed to have bitten them. Hintermayer[25] (1846) speaks very positively on the subject. He studied an epidemic of anthrax which raged amongst the deer in the Park of Duttstein in 1846. Biting flies were exceedingly numerous that year, and he considered them unquestionably the carriers of the virus and one of the causes which led to the extension of the disease. The flies (*Tabanus bovinus, T. pluviatilis* and *T. coecutiens*) assembled "usually in thousands, on the carcasses of the fallen animals, sucked the profluvia which escaped from the mouth, nose and vent, and leaving the bodies immediately sought the healthy animals, thrust their proboscides soiled with the virus into the surface of the skin, and in this way inoculated the poison of the disease." In the case of three cows, he was convinced that infection resulted from the bite of *T. bovinus*. "I examined the swellings," he writes, "very carefully when they first appeared, and found that in the center of the beginning carbuncle, a wound was present, as if the animals had been stabbed with a needle." Virchow[30] (1855) believes, in view of the experience gathered, that we must accept the possibility of horse-flies, and the like, transmitting anthrax. He believes that other flies, which are not capable of biting, are also able to carry the infectious agent on their feet and proboscides and of depositing it on the skin. Budd[32] (1862) holds a similar opinion regarding biting flies. He writes, "it is a mode of inoculation obviously difficult to demonstrate—but in proof of which numerous cases, and some apparently entirely free from ambiguity, have been recorded." He mentions two cases where anthrax was believed to have resulted from the bites of gnats. Budd[33] (1863) considered that next to eating meat of anthracic animals the greatest number of cases are caused

by fly-bites, the infectious agent "being inoculated by insects which have previously been in contact with animals or carcasses of animals affected by the disease." (Formerly anthracic meat was often sold in England. Of the 24 cases described by Budd, 20 were affected on the lip or in the vicinity of the mouth.) The greater the number of insects the greater the danger. This mode of infection might be very frequent in Burgundy and also in Siberia and Lapland, where insects "of the mosquito tribe are the great pests of the traveler." Budd states that in Lapland the popular belief prevailed, that malignant pustule was caused "by a peculiar insect which suddenly descended from the air and as suddenly disappeared." [1]

Davaine[34] (1868) wrote: "This infinitesimal quantity of blood which suffices to transmit the anthracic disease corresponds with the inoculation of malignant pustule through the proboscides of flies. It also gives us grounds for the belief that the infection of anthrax, so difficult to explain, might often be transmitted in the same way in herds." He writes later[39] (1870): "The rôle that flies play in the transmission of anthrax from animals to man has long been known." Six years before, he had made observations on the spoiling of fruits and vegetables which, he says, he traced to flies that carried the spores of Penicillium and Mucor and infected the wounded places on apples, etc., the juice of which they sucked. If they are able to do this, and carry the pollen from flower to flower, they are surely able to carry a virus. Davaine goes on to state that anthrax is worst in hot summers, but that it may also occur in cold winters, not in the fields, but in hot stables, where flies may be found all the year round. He had never seen anthrax transmitted in stables and sheep-pens in Paris, and this he attributes to the absence of biting flies, which are so numerous in the country. The disease may be communicated at a distance, but this is limited to the movements of the flies which do not go far, etc., etc. Davaine gives many reasons which have been quite differently explained since Koch's studies on the etiology of anthrax appeared. Davaine[40] (1870, II) suggests that anthrax is not more rapidly communicated by flies for the reasons that the number of biting flies is variable, that the bacilli only appear in the blood of animals shortly before their death, that the biting flies do not suck from dead animals (?) and that these flies are not nocturnal. The bacilli appearing in the blood shortly before death makes it only possible for the flies to infect themselves during that time, and they would have no chance if the animal died during the night. Gross[41] (1872) states that in a cattle epidemic which occurred in Louisiana in 1851 the "green carrion fly" communicated the disease in a number of cases to human subjects, but he gives no details.[2] The green meat-fly (*Lucilia Caesar* [L.]) is as incapable of biting as the house-fly, so Gross was mistaken as to the character of the insect. Bollinger[44] (1874) con-

[1] Budd says that in 1860 it was reported in the *Times* that 400 persons had lost their lives in Southern Russia and the province of Kiew from the sting of a venomous fly which came from Asia. It had made its appearance in the same country 60-70 years before. Budd cites cases of rapid deaths following the bites of insects, but there is no proof that they were due to anthrax.

[2] I am indebted to Dr. J. H. Wright of Boston for kindly sending me this reference.

siders that the great spread of anthrax in certain years depends on the higher temperature attained, and the consequent increase in the number of insects which serve as carriers of the infection, all the hot years of this century (1803, 1807, 1811, 1822, 1826, 1834 and 1874) having been so-called anthrax years. Mégnin[42] (1874) says that there is no absolute proof, though the idea prevails generally, that fly-bites cause anthrax. Davaine had even claimed that flies were the sole agents in spreading anthrax through herds. It had, however, been objected that anthrax occurred in winter, both in and out of the stables, when no flies were to be seen. Still, flies may play a role in warm weather. He considers the experiments of Raimbert[37 38] and Davaine[34 39 40] (1869, 1870) inconclusive. Mégnin[46] (1875) cites a report, made by Tisseraint of Lyons in 1865, of a fatal disease amongst cattle, attributed to the enormous number of mosquitoes about Lyons that year. In 1869 Mégnin saw horses suffering very much from insects, especially from the same species observed by Tisseraint. Though the animals were terribly bitten the effects were not those described by the latter author. Mégnin thinks that Tisseraint's animals suffered from anthrax, and believes horse-flies and mosquitoes may inoculate anthrax. Strauss[54] (1887) also holds the opinion that flies may carry the disease from diseased animals and inoculate healthy ones by their bites. He cites no cases. He says that the primary lesion often leads to misconceptions in this respect. W. Koch[45] says that physicians who have been in the Russian steppes refer most cases of anthrax, occurring during the harvest, to the bites of insects. Joseph[55] (1887), as the result of 30 years' experience, has come to be very sceptical regarding the rôle of flies in anthrax. Referring to the cases recorded in the literature, he denies that most of them possess any scientific value whatever, characterized as they are by many false observations and gratuitous assumptions. Joseph believes that non-biting flies (*M. domestica*, etc.) may carry the bacilli and deposit them on wounds, these latter being necessary. He does not record a single case of anthrax as due to the bite of a fly, and states how common the false belief is among laymen that the house-fly is able to bite. He tells of a case he had in 1852 of a woolsorter who claimed that a house-fly (which he showed J.) had bitten him, whereas his hand had without doubt been previously infected by a scratch due to a splinter whilst handling infected wool. Joseph examined 300 *Stomoxys calcitrans*, 100 *Hæmatopotes pluviales* L. and various species of *Tabanus* and *Chrysops* for anthrax bacilli, but always with negative result, and he never saw any of these flies feeding on the carcasses of animals dead of anthrax. Zuelzer[56] (1888) cites no cases, but asserts that flies often serve as carriers of the virus. Anthrax prevails during the hottest months (August-September)—when insects are numerous. Blanchard[202] (1890) refers to Davaine's experiments as proving that non-biting flies, belonging to the type of the common house-fly, are capable of carrying and depositing the virus on the skin of healthy animals or on food, thus giving rise to infection. The experiments of Grassi also showed that the eggs of *Taenia*, *Trichocephalus* and *Oxyuris*, as well as the spores of *Botrytis*, pass uninjured through the alimentary canal of flies. The same has been proved for the *Bacillus tuberculosis*. He considers that *Stomoxys calcitrans* (Geoffrey) may transport and inoculate anthrax or other diseases with its proboscis. This can also be said for the various species of *Tabanus*, and the same has been claimed for mosquitoes. Nörgaard[59] (1893), who investigated an epidemic of anthrax

in the state of Illinois, says he believes most of the cutaneous anthrax in animals results from the bites of flies. One of the prophylactic measures recommended by the Department of Agriculture is to closely house the animals in darkened stables to exclude flies. It is also advised to keep work-horses covered as far as possible with sheets whilst working. No cases of the personal observation of fly-bites causing anthrax are recorded.

In other cases anthrax resulted from the bites of flies which were crushed on the spot subsequently affected. These cannot be reckoned to the cases where the bite is stated to be the cause, for assuming that the insect had previously fed on infected matter, the fact of its being crushed, and its virulent contents being rubbed into the wounded skin, would account for the infection taking place. It would seem, then, that the very natural tendency to crush a fly that is biting one is especially fraught with danger.

It might be added that the effects of a mosquito bite are said to be aggravated when the insect is crushed on the skin. The probability here is that the saliva and poison are not removed again to the extent that they are if the insect is left undisturbed. Assuming that flies carry anthrax bacilli into the wound on their proboscides, it is quite possible that the fly, if left undisturbed, will suck them out of the wound again. It seems then at least probable that in many cases where infection is attributed to the bite, it is the crushing of the insect that has led to infection.

Siederer[23] (1839) tells of a brickmaker who was bitten on the cheek by a fly whilst sleeping in the open air. The stinging pain caused him to strike his cheek, on which he found the offending fly. The seat of the bite remained painful, and a malignant pustule developed there. Near him lay a dead sheep already partially devoured by birds. Siederer also reports the case of a woman who crushed a fly which was biting her face. She developed a malignant pustule. The viscera of a sheep, which had died of anthrax, were lying near to the place where the fly attacked her. Estradère[47] (1875) tells of a case which he saw in the summer of 1869, that of a farmer who was bitten on the cheek by a fly which he struck and crushed. The pain was immediate and severe, not subsiding on washing the part with cold water, rubbing it and applying pressure with the hand. That evening a violet-red spot appeared at the point bitten and next day a typical anthrax pustule had developed. The pustule was incised and cauterized, etc., the patient making a slow recovery. Édouard[50] (1882) tells of a man who crushed a large black fly which was biting him on the cheek. The pain was severe at first, then it subsided, but after a few hours intense pruritis followed, the seat of the bite being apparent as a small black spot. The next day a typical malignant pustule. Chauveau, who made the bacteriological examination, found *B. anthracis.*

Finally, in reading through the literature, I came across accounts of a series of cases where it is simply stated that malignant pustule developed in consequence of the bite of a fly.

Schwab[18] (1832) tells of a woman who died of anthrax 4 days after being bitten by a fly. Weiss[36] (1869) describes two cases where the patients positively said they had been bitten by flies on the places where the pustules developed. Bourguet[52] (1882) has apparently made it a rule to inquire from his patients if they had been bitten by insects. He had altogether seen 3 to 4 cases of malignant pustule following fly-bites. He concludes from his experience that "infection through the bites of flies is one of the modes of transmission of the disease, but that it is not the ordinary mode." Budd[32 33] (1862-3) cites two cases of infection attributed to fly-bites, on the strength of which he certainly generalizes too freely. Wuttge[16] (1828) tells of a shepherdess who died of anthrax two days after she was supposed to have been bitten on the eyelid by a fly. Of 19 cases of anthrax occurring in Prussia in 1872-1873 (Virchow-Hirsch Jahresbericht, Vol. II, 1874, p. 692), one was attributed to a fly acting as carrier of the infection. Oemler[49] (1876) records eight cases, however, where the insect accused had not been seen and other modes of infection were not excluded. Griffin[53] (1884) reports the case of a young man who was bitten on the cheek by a large fly whilst eating his dinner in a restaurant. "The fly, which was a common green bottle-fly, was killed on his cheek by a friend who was dining with him. . . . The fly had bitten sufficiently to draw blood, and it was from this point as a focus that the malignant pustule began its career." It was found on inquiry that the employees of the restaurant had been in the habit of throwing waste scraps of meat and other refuse into the back yard, and this having been stopped by order of the Board of Health it was noticed for several days afterwards that flies swarmed about the restaurant, "annoying all by their savageness." Griffin diagnosed the case as one of anthrax on the strength of the clinical symptoms alone, no microscopical examination nor inoculations on animals being made. Griffin refers to Gross (see above) as stating that the same fly had previously been observed to convey anthrax.[1] It could not have been a "common green bottle-fly," as Griffin states, as this fly (*Lucilia Cæsar* [L.]) is incapable of piercing the skin. Macleay (quoted below) also stated that this fly had been accused of transmitting anthrax in New Caledonia together with *M. domestica* (!) It is impossible to say what green blood-sucking fly was taken for a "green bottle," but the cases in which the house-fly is said to have bitten are attributable to some species of *Stomoxys*. In a letter, dated October 18, 1898, Dr. L. O. Howard, entomologist to the U. S. Department of Agriculture, informs me of the case (not published) of a young lady who died 5 days after being bitten on the lip by a fly. "Some of the blood and pus were examined and showed rod bacilli, which were decided to be those of anthrax." In a number of cases of anthrax, attributed to the bites of flies, the skin was either certainly or probably already infected. Men engaged in skinning anthracic animals particularly fear the bites of flies. It is impossible to

[1] Dr. J. H. Wright had the kindness to make an abstract of Griffin's publication for me.

draw conclusions in such cases as to the part actually played by flies; they may simply cause a wound into which the bacilli already present in the skin gain access. On the other hand, flies which may have settled on the cadaver are continually disturbed while the skin is being removed, and they may soil themselves more than usual with infected blood, etc. Gontard[3] (1763) reported the case of a man who was bitten on the hand eight days after he had skinned a number of cattle dead of anthrax. Two carbuncles appeared at the place bitten. Bourgeois[31] said he had often met with cases of anthrax in persons living near tanners and fellmongers. In one case he saw anthrax result from a gad-fly which came out of a fleece of wool. Walz[10] (1803) stated that knackers very easily acquire anthrax if they are bitten by flies while skinning carcasses. A frequently cited case is the one recorded by Siederer[25] (1839)—that of a man who was bitten on the arm by a flea whilst he was carrying home a piece of meat (from an animal dead of anthrax) with which to feed his dog. He rubbed the place where the flea had bitten him, with his soiled hand, and a malignant pustule subsequently formed on the spot. In the same category no doubt belongs the case reported by Thomassin[6] (1780-1782) of a woman who developed anthrax (?) in consequence of a bee's sting. Bollinger[44] (1874) reports a case which occurred in the Bavarian Alps, where a man acquired anthrax by being bitten by a fly whilst engaged in a post-mortem on a cow. In another case this mode of infection was probable. (See Koch.) Majocchi reports the case of a man who was bitten on the leg whilst watching an anthracic animal being skinned. A malignant pustule developed at the spot bitten. Estradère[47] (1875) tells of a Spaniard who was bitten on the outer corner of the eye whilst skinning sheep dead of anthrax. He immediately experienced a sharp pain, left his work and washed his eye. A malignant pustule developed at the seat of the fly's bite. Macleay[51] (1882) gives the case of a butcher who was bitten on the ear by a fly and died of anthrax. He was bitten whilst in his slaughter-house. Layard, who sent him the notes on the case, had been bitten three times by flies (*Stomoxys*) and described the pain as immediate and severe. Many anthrax cases attributed to bites from *M. domestica* and green bottle-flies occurred at this time in New Caledonia.

Experimental.

The first experiments to determine the rôle of flies in the spread of anthrax were made by Raimbert[37] (1869). He placed biting flies (*Tabanus*, *Haematopota* and *Stomoxys*) beneath a bell-jar containing a vessel filled with dried anthrax blood to which water had been added. None of the flies drank the fluid. He did the same with the house-fly and meat-fly. These drank the fluid and soiled their bodies, wings and legs with it. He saw anthrax bacilli in preparations made of the proboscides two hours after the flies had been introduced into the bell-jar and later observed them in the excreta. In another experiment he left meat-flies 12 to 24 hours in the apparatus and then inoculated their legs, wings, proboscides,

etc., into guinea-pigs. The latter died of anthrax. He concludes from the latter experiments that flies which have come in contact with animals dead of anthrax or their refuse, on which they have fed, are able to transmit the anthrax virus and deposit it on the skin of susceptible animals. With regard to his experiments on biting flies (which gave no result whatever, as they did not drink the blood in the apparatus, and he does not state that he tried to infect animals by allowing the possibly infected flies to bite them), he comes to the totally unjustified conclusion that these are "not very probably the agents of the inoculation of the virus of anthrax." Davaine[39] (1870, I) made similar experiments. He inoculated guinea-pigs with the proboscides, legs and wings of flies removed directly from the bell-jar. The animals naturally died of anthrax.

After allowing flies to drink anthracic blood for 24 hours, he replaced the latter by sugar-water. Of 7 guinea-pigs inoculated with parts of flies which had not had anthrax-blood for 40 hours to 3 days, 4 died of anthrax and 3 survived. He used *Musca vomitoria* for these experiments. He concludes that various flies may infect wounds, but believes that species of *Tabanus*, and especially *Stomoxys*, infect by their bites. "This has not been proved experimentally, but the analogy proves it clearly." He believes they inoculate directly from animal to animal, and that they constitute the most important means of communicating anthrax. He expresses surprise in consequence that anthrax is not more fatal. Bollinger[48] (1874) gathered flies (Bremsen) off of a cow dead of anthrax and saw the bacilli in preparations made from the stomach and intestine of the insect. Two rabbits inoculated therewith died of anthrax. He concludes that they may act as agents for conveying anthrax from diseased animals to man and healthy animals. Bollinger[41] (1874, II) proved that flies did not die, as was supposed, from being fed on anthracic blood. Mégnin[42] (1874), referring to the experiments of Raimbert and Davaine, above mentioned, says *M. vomitoria* with which they experimented does not go near living animals whether healthy, wounded or sick, contrary to biting flies, which never go near dead bodies or even to those animals that are seriously ill. (This statement is certainly wrong). He, however, justly remarks that the experiments prove no more than that *M. vomitoria* is a receptacle for the virus. In August and September, 1874, Mégnin had occasion to see biting flies attack "very

sick" animals, and believes they may communicate infection to those that are healthy. He saw *Stomoxys* drinking the excretions emanating from the leg of a horse suffering from erysipelas with gangrene. He took their proboscides, and inoculating them into healthy horses, produced the same effects as with inoculations made with the excretions themselves. The proboscides contained bacteria similar in appearance to those seen in the wound. He made the same observation on a species of *Simulium*, which at times attacks animals in clouds, and to the agency of which a fatal disease in cattle was attributed in 1865—a disease which Mégnin thinks was anthrax. Mégnin thinks his observations demonstrate that biting flies (*Stomoxys*, *Simulium*, *Glossina*, etc.) may at times cause infectious diseases, including anthrax. (His experiments, of course, are far too superficial to justify any such general conclusion.) Celli[111] (1888) reported experiments made at Palermo under his direction by G. Alessi, in which flies had been fed with a pure culture of *B. anthracis*. The fly contents and dejections were examined microscopically and culturally, and inoculations made therewith on mice, guinea-pigs and rabbits, proving that the flies contained and gave off virulent anthrax bacilli in their dejections. No details whatever, more than I have cited, are given.

Railliet (Zool. méd. et agricole, 1895, Paris, p. 786) sums up the matter regarding the rôle of biting flies with appropriate words. He says it is *conceivable* that the proboscides of *Stomoxys* and similar flies may inoculate septic organisms, having previously become contaminated on cadavers or diseased animals. "Nevertheless, no direct proof has been given as yet in favor of this view; the artificial inoculation of the proboscis purposely infected can evidently not give any indications of serious value." It seems to me perfectly absurd that any value should have been attached to such experiments. When the insect sucks blood, it injects uninfected saliva, and sucks up the bacteria that may adhere to its proboscis. As Railliet says, it is conceivable that infection may occur, but it is probable, when we consider the process, that infection is the exception and not the rule. It would be really advisable to make some experiments with biting flies, such as I have made with *Cimex* (see below). Only judging from a trial I have lately made, it is not so easy to manage with flies as one would suppose. The fact that I was never able to produce infection through the bite of in-

fected bed-bugs, in experiments made with anthrax, plague, chicken cholera and mouse-septicemia, is certainly suggestive. Still, it may be otherwise with biting flies, especially the larger varieties, when greater entrance wounds are made by the proboscides and the mechanism of blood-sucking is possibly different. We know that there are other and much more important ways by which infection may occur—ways which have been rendered clear since Koch published his classic researches on the etiology of anthrax. If it were anything like the rule that infected flies produce anthrax, I believe the mortality would be still greater than it is. It does seem high time, though, after nearly a century and a half of discussion, to see what would be the result of properly carried-out experiments. That ordinary flies (*Musca domestica* and the like) may carry about and deposit the bacillus of anthrax in their excrements, or cause infection through their soiled exterior coming in contact with wounded surfaces or food, may be accepted as proven in view of the experimental evidence already presented.

The Rôle of other Insects in Relation to Anthrax.[1]

Coleoptera.

Proust[57] (1894), in examining goatskins taken from anthracic animals, found quantities of living *Dermestes vulpinus* upon them. He found virulent anthrax bacilli in their excrements, as also on the eggs and in the larvæ. It is evident from this that these insects which feed on the skins permit the anthrax spores to pass uninjured through their alimentary tract. Heim[58] (1894) also had occasion to examine some skins which were suspected of having caused anthrax in three persons engaged in handling the leather. He found the larvæ of *Attageus Pellio*, *Anthrenus museorum* and *Ptinus*, also fully developed insects of the latter species on the skins. All these insects had virulent anthrax bacilli (spores) on their surface and in their excreta, from which Heim concludes they

[1] The occurrence of anthrax in years when grasshoppers have been very numerous has been noticed in France by Regnier and in Germany by Seiler. A similar coincidence has been observed with regard to caterpillars by Seiler in Germany, by Scheuchzer (1732) in Switzerland and Haartman (1756-1758) in Finland. As Heusinger[29] (1850), who cites these observations, very properly remarks this as only a matter of coincidence attributable to the fact that anthrax is worse in hot years, the high temperature also favoring the greater multiplication of all insects.

might spread the disease. He says the excreta are very light and easily scattered by the slightest current of air. Heim does not believe the bacilli multiply in the bodies of these insects, but that the latter may be dangerous through their scattering the spores about.

Cimex lectularius.

Nuttall[99] (1898), in consequence of statements made by different authors that the bed-bug (*Cimex lectularius*) is capable of causing infection by its bite in plague and other septicemic affections, made experiments with bed-bugs by letting them bite animals that had just died or were dying of anthrax, plague, chicken cholera and mouse-septicemia, and then transferring them to healthy animals. Mice were used for these experiments because they are most highly susceptible to these affections, it having been calculated that the inoculation of a single anthrax bacillus or but a few bacilli of the other species is sufficient to cause a fatal disease. In each experiment the number of anthrax bacilli by control bugs was determined by microscopical countings or cultures. The mice inoculated with anthrax culture died after 18 to 24 hours. They were placed in glass-covered dishes and hungry bugs were allowed to attack them. As soon as some of the bugs had sucked a little blood, which was evident by examining them by transmitted light, they were removed to test-tubes by means of a small camel's-hair brush and transferred to a shaved spot on healthy animals, the bugs being kept in place by inverting and applying the mouth of the test-tube to the skin of the mouse. The infected bugs being transferred immediately to the healthy mouse was a condition most favorable for a successful infection to take place, providing the bugs were capable of transmitting the disease by the act of biting. *The results were entirely negative.* Eight mice bitten by 124 infected bugs all remained healthy. Two mice were bitten by 6 infected bugs, which were struck (but not crushed) whilst sucking, the idea being that perhaps some of the anthrax bacilli they contained might be forced back through the proboscis into the wound. The result was negative. The crushed spleen of an anthracic mouse was rubbed on the backs of eight mice by means of a bit of filter paper, the hair having been cut short at that spot. Four of the mice were bitten by six bugs with negative result. Summing up, we find that the bites of 136 infected bugs were without result. It was further shown that

anthrax bacilli die off in the bug's stomach more rapidly at high than at low temperature, in consequence of the increased physiological activity of the insect at the higher temperature, the bacilli being more quickly digested. All the bacilli were killed off in 48 to 96 hours at 13 to 17° C., and in 24 to 48 hours at 37° C. Inoculations made on mice with the contents of bugs gave a similar result. The dejections of bugs fed on anthrax blood only contained living bacilli during the first 24 hours after feeding.

In view of these experiments, the writer concludes that infection through the bite of a bug either does not occur or is exceptional. That infection might occur if the bug were crushed (within a reasonable time after it had infected itself) and the part scratched is self-evident. We are speaking here strictly of infection through the *proboscis* of a blood-sucking insect.

Since the above was written, Joly[137] (1898) kindly sent me his dissertation recently published in Bordeaux, wherein he describes similar experiments that he had made. In one experiment he rubbed up anthrax culture in human blood and placed 5 bugs in the infected fluid, which they imbibed. After a short interval he placed them on a rabbit's ear, but they would not bite. The next day, and on four successive days, they were again placed on the rabbit's ear, which they bit and from which they sucked blood. The result was negative. In a second experiment he bathed 3 bugs in anthrax culture and placed them some hours later on a rabbit's ear. One bug sucked blood. The bugs were placed on the rabbit's ear on 3 successive days. The result was also negative. In a third experiment, which more properly simulated natural conditions, he placed 6 bugs on an anthracic rabbit whose blood contained bacilli. The bugs sucked themselves full of blood. On the next, and on five successive days, the infected bugs were placed on healthy animals, whose blood they sucked. Here, again, the result was negative.

Pulex.

A rôle having also been attributed to fleas in the spread of various septicemic affections, Nuttall (ibid.) further experimented upon the fleas which are found on the gray mouse. The experiments are unfortunately few, in consequence of the fleas having been scarce. Nine fleas were removed from a mouse dead of anthrax and placed on two white mice. Both of these remained alive. The

contents of 4 fleas were examined microscopically (stained with methylene-blue) immediately after their removal from mice dead of anthrax. Six bacilli were found on an average in ten fields. Nearly all the bacilli showed marked signs of degeneration (death). One examined 24 hours after removal showed 3 bacilli in 10 fields, another examined after 120 hours showed none. Cultures from 3 fleas made immediately after removal yielded one anthrax colony; all cultures made after 24 hours or more were negative. The contents of 7 fleas inoculated into 3 mice, 8, 12 and 24 hours respectively, after their removal from mice dead of anthrax, gave negative results.

It seems, then, that anthrax bacilli die off rapidly in fleas, and the conclusion appears justified that they cannot play much of a rôle, if any, in the spread of this disease.

Plague.

It has been claimed for a variety of insects that they may serve to spread the plague. The earliest mention that I have found of the presence of insects in connection with plague is in "De regimine pestilentico," which appeared in 1498, and was attributed to Bishop Knud of Aarhus in Denmark, where it is stated that the first signs by which one may foretell the approach of plague are frequent changes in the weather during the summer, much fog and rain, the appearance of many flies, etc. In a publication entitled "Tractatlein von der Pestilenz," by Varwich (1577), the author states that in the plague year, 1576, the summer was exceptionally hot, and large numbers of flies were observed there as well as in England. Diemerbroeck (about 1646), who described the plague in Nimwegen, Holland, says that its coming was announced by meteors, swarms of insects, etc. These three references are taken from Mansa[61] (1872-3). I am indebted to my friend Dr. N. P. Schierbeck, Privatdocent in Copenhagen, for the abstracts. Haeser (Geschichte der med. und epidem. Krankh., 3 Aufl., vol. iii, 1882) states that the city of Bengasi, in Tripolis, was visited severely by the plague in 1858-1859 and lost two-thirds of its inhabitants by this disease. Bengasi had a population of 10,000, was very filthy, and was known as the "Kingdom of Flies" among the Turks, in consequence of the enormous number of these insects

that were to be found there. In 1894, Yersin[62] observed many dead flies lying about in the laboratory (at Hong Kong) where he was accustomed to make autopsies on the animals that died of plague. Taking one of these flies and removing the head, legs and wings, he crushed the insect in bouillon and inoculated a guinea-pig with it. The fluid inoculated contained many bacilli, presenting an identical appearance with those of plague. The guinea-pig died in 48 hours of plague. He concluded that flies are susceptible to the disease, and are capable of spreading the infection. It seems this was the only observation he made, and it appeared to me not to carry conviction, for to begin with, it was but a *single* fly that he examined and no experiments were made of feeding flies with the bacillus. We often see dead flies lying about in closed rooms, especially when the weather is hot, many dying, no doubt, from lack of water, and it also seemed possible that Yersin's flies might have been drinking sublimate solution, of which there must have been plenty at hand. The fact that the *one* dead fly which he examined contained plague bacilli certainly does not prove that the flies died of plague. Nuttall[67] (1897) made a series of experiments on flies (*Musca domestica*) which conclusively proved that flies are able to carry the infection, and that they die of the disease. He placed flies in a suitable apparatus, and fed them on the crushed organs of animals dead of plague, control flies being fed on similarly prepared organs of uninfected animals. The insects were kept under precisely the same conditions. In one experiment at 12 to 14° C., all the flies were still alive after 8 days. In another experiment at 14° C., all the infected flies (9) had died by the 7th day, whilst only 2 out of 10 controls had succumbed. In a third experiment at 14° C., all the infected flies were dead on the 8th day, whilst 6 of the 14 controls had succumbed. In the first experiment it was observed that no flies died (with the exception of two weakly ones) within the first 48 hours; in the second experiment none died within 72 hours. In the last case they had only received infected food during the first 48 hours; in the preceding experiment this had been renewed every 24 hours. At higher temperatures the flies died more rapidly, mostly within 3 days when maintained at 23 to 28° C. The fact that infected flies can live for several days points to the possibility of their playing no inconsiderable rôle in the spread of plague, for they would have plenty of opportunity to

gain access to food into which they might fall and die, or on which, in again feeding, they would deposit their excreta laden with plague bacilli. Experiments showed that the flies contained virulent bacilli 48 hours and more after they had been fed on infected organs and had been kept in clean vessels. The practical applications that should be made of the knowledge here acquired readily suggest themselves. The bodies of persons dead of plague should be covered as quickly as possible with sheets moistened with disinfectants; dead animals should be quickly disposed of and all excreta promptly disinfected. Food should be kept covered, and everything done to keep away flies. Ogata[66] (1897), who suspects flies, fleas and mosquitoes of aiding in the spread of plague, suggests the advisability of protecting plague patients by mosquito nets.

That other insects besides flies may play a part in the spread of plague has been claimed by various writers. Hankin[63 64] (1897) in India killed rats and mice by inoculating them with the excreta of ants (*Monomorium vastator*) which had previously devoured rats dead of plague. Hankin thinks such ants may spread the plague by gaining access to the bath-rooms, etc., in search of water, their fæces being deposited there. He found that ants neither died of plague nor retained the infection for any length of time. In some cases he found ants from localities in which rats were dying of the disease to be infected, " but in other localities in which a severe epidemic was going on among human beings, but in which there was no evidence of the death of rats, ants were always found to be free of infection. In India ants will eat up a rat dead of plague with extraordinary rapidity, and it cannot be denied that by thus disturbing and carrying about infected material they may increase the risk of infection from dead rats." Ogata[66] found plague bacilli in fleas taken from rats dead of plague, and thinks such fleas may cause infection by their bites. Mosquitoes and bed-bugs have been similarly blamed without there being any facts upon which to base the opinion. The German Plague Commission[65] (1897) were unable to determine whether any infections arose from the bites of insects. They thought the mosquitoes did not inoculate the disease, because those in attendance at the Plague Hospital, whilst severely bitten, would have been more frequently attacked. They believed that the constant *scratching of the skin*, in conse-

quence of the bites of vermin, sufficiently explained the frequency with which the lower classes are affected by the plague. They also found that fleas taken from rats dead of plague contained virulent bacilli, as was proved by the inoculation of their contents into a guinea-pig. Yamagiwa[68] (1897) mentions a case he observed where an ulcer formed at a spot where a bed-bug had bitten the patient. The latter acquired the plague, the infection apparently starting at that point. He does not say that the bite of the insect caused the disease, but that the wound served as a port of entry. Sticker[69] (1898) blames everything resembling insects with spreading plague, but gives no facts. According to Sticker, ants (in this he probably intends to refer to Hankin's observations) may gain access to man and infect him, also the Pediculi that are found on rats and possibly their acari, etc.

It seemed advisable, in view of these various statements, to study the matter experimentally. (The writer was unfortunately obliged to break off his experiments in this direction before they were completed in consequence of all experimental work on plague being forbidden in Prussia soon after the German Plague Commission left for India.) Bed-bugs were allowed to suck blood from rats and mice dying of plague, and their contents were inoculated at stated intervals into mice. This series of experiments showed that the bacilli died off rapidly after being 24 hours in the stomach of the bug; all being dead after 5 days. 22 bugs which had just sucked the blood of a mouse dying of plague (the blood contained many bacilli) were immediately placed on 4 mice. None of the mice sickened after being bitten by the infected bugs. In view of these few negative results a similar series of experiments was subsequently carried out with animals infected with anthrax, chicken cholera and mouse septicemia without a single positive result being obtained. I think for this reason the conclusion is justified that if the bug-bite is a cause of infection it must be unusual. On the other hand, it is quite possible that a person crushing an infected bug, and scratching the spot where the insect has bitten, may thus inoculate himself with plague bacilli; this, however, would not take place if a sufficient interval of time had elapsed after the bug had sucked blood containing the bacilli.

Simond[70] (1898, pp. 668-677) having noted the frequency with which persons who have handled rats dead of plague in India

acquire the disease, attributes their infection to the intermediation of the fleas which abandon the rats after they have died. Not more than one rat in a hundred, thus handled, may give rise to plague in man, but the rats which are considered to have caused infection had almost always died but a short time before. "It is usually in the morning that the carcass of a rat which has died in the night is fatal to him who touches it. We were unable to discover a single case of a rat whose death had occurred 24 hours previously, having communicated the plague." According to Simond, then, the danger of handling rats dead of plague would be confined to but a few hours following its death. The relative difficulty of producing infection by feeding, and the ease with which plague is induced by the subcutaneous inoculation with minute quantities of virus, lead Simond to assume that infection usually takes place through the skin. Whilst a place of entrance cannot be found in animals, this is not the case in man, for in about one case in twenty of human plague subjects, Simond found one or more phlyctænæ present. These primary lesions are painful, are evident prior to the development of any other symptoms, and last to the end. They always contained plague bacilli, even after suppuration had set in, were invariably accompanied by a bubo in a corresponding situation, and only affected parts where the skin is delicate. (Simond cites 61 cases in this connection.) Simond states that Sticker, as also two Japanese physicians who acquired plague from pricking themselves with the point of an instrument at autopsies on plague subjects, presented similar lesions to those above-mentioned at the point pricked.

Simond found that fleas taken from rats and transferred to human subjects and dogs proceeded to suck the blood of the latter. Healthy rats, and rats kept in the laboratory, exhibit few fleas, but the contrary is the case in sick rats which no longer make the effort to clean themselves and keep off these parasites. He found bacilli in fleas taken from rats dead of plague, which presented the microscopical appearance of plague bacilli. Such bacilli were absent in fleas removed from healthy mice. Simond removed fleas from rats dead of plague, crushed them, rubbed them up with water and inoculated 3 mice with the fluid. One mouse died of plague in 80 hours, the other two died on the 9th and 12th days respectively, but no bacilli could be found in them. [So it is doubt-

ful what they died of—N.] In another experiment he placed 20 fleas (obtained from a cat) in a bell-jar with a rat dying of plague. He then placed a healthy rat in a cage into the bell-jar, but also allowed the cadaver of the first rat to remain 36 hours in the vessel. The second rat died on the fifth day of plague. This experiment was repeated three times, once with mice, the result being positive, twice with rats, the result being negative. Simond attributes the negative result to the rats catching and devouring the fleas which attacked them. He had never observed plague pass from diseased to healthy animals when the former were free from fleas, in support of which statement he, however, only cites a single experiment in which a flealess cadaver of a plague-rat remained 24 hours in a cage occupied by 7 healthy rats. (He does not state how long these were kept under observation.) Simond does not directly claim that fleas inoculate the bacilli by means of their proboscides, but he certainly implies it. He observes that he has noticed fleas voiding their dejections on the skin whilst in the act of sucking blood, and thinks if bacilli were in their excreta these might readily gain an entrance into the wound produced by the insect and thus give rise to infection. He believes that the different forms of spontaneous plague in man and animals are usually attributable to the agency of parasites, chiefly fleas, and thinks his hypothesis, for such it must still be called, explains the prevalence of plague, especially in filthy dwellings. Simond believes that infection from man to man takes place but in an insignificant number of cases as compared to those where fleas carry the infection from rat to man. In conclusion, he suggests among other prophylactic measures the advisability of throwing scalding water on dead rats so as to kill the fleas on them prior to removing the carcasses. He regards rats as the main cause in the spread of plague among human subjects, and would appear to have made some observations, which show that rats continue to die throughout the duration of plague epidemics, though it is only when the mortality is great amongst them that it is especially noticed. Simond also believes that *Cimex* may convey infection from man to man.

Simond does not seem to have been aware of the experiments made by Nuttall with fleas and bugs, or he would not have stated that the virulence of the bacilli may be increased in the body of the flea. The fact that various germs were seen to die off in

Nuttall's experiments with these insects certainly should check any tendency to accept Simond's generalizations until more work has been done on the subject. What we want in this respect is more facts and fewer opinions, and the facts can only be gathered by further experimental research. Simond does not seem to know (he says as much) that the fleas which infest rats and mice belong to a *different* family from that which attacks man, and, though it is quite possible that they may suck human blood in a laboratory experiment, it seems to me open to question that they would do so under natural conditions. It is true that Lucet showed that the bird-flea (*Pulex avium*, O. Taschb., 1880) may bite man severely, whilst *Pulex irritans* has been found on the dog, cat, and even on the rabbit and once on the horse (Railliet). The dog- or cat-flea may also attack man, and Railliet has found it on rabbits, though he was unable to maintain them in rabbit-hutches into which he had introduced them in great numbers. (See Railliet[242], 1895, pp. 802-805.) Baker[1] (1895), who states that there are 47 species of fleas known, says that *Pulex serraticeps* has been found on wild dogs and cats, on *Herpestes ichneumon* (Pharaoh's rat), *Faetorius putorius* (common European polecat), *Hyaena striata*, *Lepus timidus*, and *Procyon lotor* (raccoon) as also on man. Howard[328] (1896) says that this species often attacks man in damp summers in the Eastern States (New York, Baltimore and Washington) *Pulex irritans* being absent. I find no references in the literature to the effect that the rat- and mouse-flea (*Typhlopsylla musculi* Dugès) will use man as a host; it is nevertheless possible, especially when, as at times in plague epidemics, their natural hosts are dying off rapidly in and about human dwellings.

Hog-Erysipelas and Mouse-Septicemia.

Marpmann[105] (1884) says that the peasants in Friesland believe that during epidemics of hog-erysipelas the disease is spread from one pig-sty to another through the agency of flies. For this reason some owners purposely darken their pig-sties so as to keep out the flies, it being claimed that hogs kept in a darkened sty remain healthy. He made no experiments with the *Bacillus erysipelas suis*, but, during May and June, examined 230 flies by making

[1] Baker, C. F., Canadian Entomologist, 1895, p. 221-222, cited by Howard, 1896.

cover-glass specimens from the fluid squeezed from the proboscis and anus, finding cocci and bacilli (not stated which kind) in all of them. He also fed flies with nutriment containing the *Bacillus prodigiosus* and *B. foetidus*, observing that these bacteria appeared in the excreta alive and uninjured. His experiments, of course, do not prove anything for hog erysipelas. He reasons that, because a rôle has been attributed to flies in anthrax, they probably play a rôle here. He refers to the observations of Grassi, quoted elsewhere.

Nuttall[60] (1898) allowed bed-bugs to suck the blood of mice dying of mouse-septicemia, and at stated intervals inoculated mice with their contents. Mice thus treated died in 78 to 79 hours when inoculated with the contents of bugs removed 24 hours after they had infected themselves. After 46 to 72 hours had elapsed the mice died in 96 to 99 hours. One survived after being inoculated with the contents of two bugs after 96 hours. Two mice died in 112 to 116 hours when inoculated with the contents of 4 and 3 bugs respectively after an interval of 120 to 144 hours. One mouse inoculated with the contents of four bugs after 240 hours survived. It is evident from this that the bacilli die off gradually in the bug's body. Five fleas removed from a gray mouse dead of the disease were transferred to a healthy animal. The latter remained healthy. No experiments with house-flies or biting flies have yet been made. Five mice bitten by 42 infected bugs remained healthy.

Chicken-Cholera.

That insects may play a rôle in the spread of this affection has, I believe, not been stated. It having been claimed that bed-bugs served as active agents in the spread of plague, Nuttall[60] (1898) included this disease in his experiments on other septicemic affections. (According to Railliet [Zool. méd. et agricole, Paris, 1886, p. 578] *Cimex lectularius* attacks brooding hens so as to force them sometimes to leave their eggs. Railliet believes, but in this he does not agree with other authors, that it is the same species which is found in swallows' nests, pigeon-houses and places where bats congregate.) Nuttall allowed 5 mice to be bitten by 66 infected bugs (see the methods described under anthrax); all of the mice remained alive. Cultures made from bugs after an interval

of 72 hours at 13 to 14° C., of 48 hours at 19° C., showed no colonies. In bugs kept at 37° C. very few bacilli remained alive after 24 hours. A mouse inoculated with the contents of two bugs after 148 hours remained alive. A flea was transferred from a dead to a healthy animal with negative result. Cultures made from 3 fleas taken from a mouse dead of the disease yielded respectively 0, 1, and 30 colonies of the chicken-cholera bacillus.

Infection with Bacillus Septicus Agrigenus (Nicolaier).

Marpmann[129] (1897) fed flies (presumably *M. domestica*) with pure cultures of the *Bacillus septicus* in peptone water. (This bacterium is allied to that of chicken-cholera.) Twelve hours after the flies had been infected, he inoculated their contents into mice. Control mice were inoculated with the contents of uninfected flies, as also with culture.

(*a*) 270 mice were inoculated with infected flies. Of these 196 (70 per cent.) died, 179 after 20 hours, 17 after 30 hours or more. All did not die of infection due to *B. septicus*, but how many did die of it is not stated.

(*b*) 270 mice were inoculated with culture. All of these died of the infection, 223 after 10 hours, 29 after 20 hours, 18 after 36 hours or later.

(*c*) 270 mice were inoculated with the contents of ordinary flies. Of these 14 died of Proteus infection.

He concludes, because all the mice in group (*a*) did not die, that the bacilli are attenuated and digested within the body of the fly. He states that those mice which survived the inoculation with infected flies had been partly rendered immune, only 42 per cent of them dying when subsequently inoculated with virulent culture. He thinks that probably all other pathogenic bacteria may behave in the same way, a quite unjustified generalization, and goes on to theorize (!) about infected flies, bugs and fleas being perhaps able to produce immunity through their bites. (The same idea lay in Finlay's mosquito inoculations against yellow fever. King also suggested the possibility of this in malaria.) Marpmann thinks immunity to diphtheria, cholera and tuberculosis might be produced this way. (We may pardon the somewhat loose theorizing, but the unexampled and wrongful extravagance of using 810 mice to so little purpose, when a tenth of that number might have been sufficient, deserves unqualified censure.)

Septicemia, Pyaemia, Erysipelas, etc.

Faure[88] (1868) reports a case of septicemic infection following the bite of an insect, the character of which was not determined. Paltauf[116] (1891) tells of the bite of a fly (species?) producing pyæmia. The patient, a young woman, was bitten on the eyelid, and twelve hours later severe erysipelas and meningitis followed, the patient dying after two days. He found enormous quantities of *Staphylococcus pyogenes aureus* and *albus* in the various organs. Chrzaszczewski[113] (1891) describes a fatal case of septicemia following an insect's bite, and states it is the fourth of the kind he has seen in his practice. He thinks this is to be attributed to the frequency with which dead and putrifying animals are left lying about in the roads, serving as places of assembly for flies. Joseph[55] (1887) saw three cases of septicemia follow the bites of *Stomoxys calcitrans* L., two of them (children aged 2 and 4 years respectively) ending fatally. It may be noted in this connection that Celli[111] (1888) reported experiments on flies (*M. domestica*, no doubt) which showed that the *Staphylococcus pyogenes aureus* was unaffected in its virulence by passage through the fly's intestine. Alessi fed flies with pure cultures of this staphylococcus, made cultures, and also inoculated rabbits and mice with cultures made from their intestines and excreta.

Berry[120] (1892) writes of a case of a man who was bitten in the eye by a fly which had apparently risen from a dung-hill. Severe conjunctivitis accompanied by extensive corneal ulceration followed 24 hours later, also general prostration lasting for months. In another case where a fly entered the eyelid, diphtheritic inflammation of the conjunctiva resulted, the cornea was destroyed and severe general symptoms supervened. Joseph[55] (1887) in a practice of 30 years has several times seen erysipelas follow the bites of *Haematopotes pluvialis* L., and he thinks biting flies may convey the specific agents here as in septicemia.

Febris Recurrens.

Tictin[132] (1897) reports that he observed many cases of this disease in the night asylums, where the people, filthy and ragged, slept on bags of straw placed on the floor. The fact that fleas, lice and bed-bugs abounded, made him suspect they might serve to spread

the infection, either by first sucking the blood of an infected individual, and immediately afterwards attacking the healthy; or, that bugs full of infected blood may be crushed on the body, the infection being then produced by scratching. The latter view seems to me tenable, judging from my own experiments. Tictin allowed bed-bugs to suck recurrens blood, then crushed them and inoculated their contents immediately into monkeys. The monkeys acquired fever. A negative result was obtained when the contents of 6 bugs were inoculated 48 hours later, and it was observed that the spirochætæ were no longer motile, though they stained normally. (Compare with the results of the writer with anthrax, plague, etc., and *Cimex*.) Flügge[112] (1891) supposed that vermin served to spread this disease.

Yellow Fever.

Nott[86] (1848) seems to have been the first to attribute a rôle to insects in the dissemination of yellow fever. He, however, does not claim the "insect theory" as his own, but he believes it applies to yellow fever as also to malaria. Speaking of yellow fever, he says it occurs at times and places and under conditions favoring the development of insects; in other words, that the natural history of yellow fever is closely allied to the natural history of insects. He considers it very likely that yellow fever is produced by germs, infusoria or animalcula, and that its spread from one locality of a city or town to another, is accomplished by the higher forms of insect life.[1] In 1881-1886 Finlay[101 106 108] of Havana, came out as the advocate of the mosquito theory of yellow fever, and his publications gained him a considerable amount of notoriety at the time. He considered that the mosquito played the chief rôle in the spread of yellow fever, and that the limits of extension of the tropical mosquito, due to temperature, accounted for the limits of the disease. He did not think that fleas and other blood-sucking insects played a rôle. He considered that immunity to yellow fever might be produced by allowing mosquitoes which had sucked the blood of a yellow fever patient to subsequently bite the individual who was to be protected. What he has to say of the habits of the

[1] I am indebted to Dr. Isadore Dyer of New Orleans, La., for an abstract of Nott's publication, kindly made at my request, the original being inaccessible to me.

mosquitoes with which he experimented might be of value to those who would wish to control Ross's observations on malaria.

Finlay worked with two species of mosquito: (1) *Culex cubensis*, vulgarly called "Zancudo," which he said was strictly nocturnal. He was unable to make it suck blood more than once, though he kept it alive 40 days with sugar and water. (2) *Culex mosquito* or *C. fasciatus*. Only the females suck blood after having paired. The lancets in the act of biting penetrate the skin to a depth of 1.5 to 2 mm. and they require 1 to 7 minutes to fill themselves with blood. When filled they are easily caught by means of an inverted glass. When they emerge from the pupa case, their lancets have often not sufficient rigidity to penetrate the skin. This species of mosquito sucked blood repeatedly, but required periods of rest of between 2 to 5 days, depending upon the season. He placed them in tubes, the ends of which were closed by muslin, so that by placing this end of the tube upon the skin the mosquitoes could suck by biting through the muslin. A female died after 31 days of captivity, having bitten 12 times and laid about 200 eggs. The eggs are laid a few days after the mother-insect has filled herself with blood and are hatched in 2 to 4 days in summer; they become converted into pupæ in 12 to 14 days, remaining in this stage 2 to 3 days before emerging as a winged insect. This occurred usually 2 to 3 weeks after the original egg was laid.

In 1891 Finlay[114] reported that he had subjected 67 persons to his mosquito inoculations since 1881. Of these 52 had been 3 to 7 years on the island and had experienced suspicious or mild yellow fever. He attempts to prove that the mosquito bites have afforded protection. In (*a*) 15 cases the observation was incomplete; in (*b*) 12 cases fever with or without albuminuria followed 3 to 25 days after the "inoculation"; (*c*) 12 remained healthy after being bitten; (*d*) 24 remained healthy 25 days, and subsequently had mild fevers "either non-albuminuric or with slight or transient albuminuria"; (*e*) 4 suffered no pathogenic effects from the "inoculation," but subsequently developed severe yellow fever, from which 3 recovered and 1 died. Excluding group (*a*), which leaves 52 cases, there was "mild acclimatization" (due as he thought to the protective effects of the mosquito-bites) in 48 (92.2 per cent), there was acclimatization with "regular yellow fever" in 3 who recovered (5.9 per cent) and 1 who died (1.9 per cent). He next (1883 to 1890) "inoculated" 33 Jesuit and Carmelite fathers that came to Havana, 32 who were not "inoculated" serving as controls. Of the uninoculated 5 died of yellow fever, the rest were protected, none dying. The inoculations with 1 to 2 recently contaminated mosquitoes are, according to Finlay, free from danger. In 18 per cent of the cases a mild attack of yellow fever is the consequence, resulting in immunity. "The contaminated mosquitoes appear to lose, either partially or completely, their contamination after they have fed on strong, healthy subjects, whereas the contamination appears to become intensified by successive stings of the same insect on yellow fever patients."

Corre[108] (1883), Sternberg[115] (1891) and others very appropriately criticise these remarkable statistics and conclusions. The experiments being made in a country where the disease is endemic makes

any conclusions impossible regarding the reaction fever following on the mosquito-bite as being due to the "inoculation"; it is, probably, simply a matter of coincidence.

Yellow fever may occur under conditions which exclude mosquitoes, etc. Hammond[118] (1886) writes that in 1839 there was yellow fever at Augusta, Ga., and none at Summerville, a suburb situated on sandhills and free from mosquitoes. Later a straight, broad road was built connecting these places, and cisterns placed along it in the swampy land. Mosquitoes now became "an intolerable pest" at Summerville, and when yellow fever reached Augusta in 1854 it also spread to the suburb. According to Mims, of Aiken, S. C., there were no mosquitoes there until they were apparently brought by the railroad. Garrin had attributed the entry of yellow fever into Augusta in 1839 to infected freight cars. Roe, of Alabama, told Hammond that he had once found a dozen or more varieties of mosquitoes on quarantined ships at Long Island, the vessels having come from infected ports.

Cholera and Flies.

That flies might be active agents in the spread of cholera was believed long before the discovery of the specific germ. The presence of large quantities of flies in cholera times is referred to by J. F.[71] (1853) as occurring at Newcastle-on-Tyne, though he does not consider they may act as carriers. He writes: "The air in certain parts of the town is literally filled with a small fly." . . . "What is to be expected from the death and decomposition of this mass of insect matter?" etc. Nicholas[72] (1873) writes that in 1849, when cholera prevailed at Malta: "My first impression of the possibility of the transfer of the disease by flies was derived from the observation of the manner in which these voracious creatures, present in great numbers, and having equal access to the dejections and food of the patients, gorged themselves indiscriminately and then disgorged themselves on the food and drinking utensils. In 1850 the 'Superb,' in common with the rest of the Mediterranean squadron, was at sea for nearly 6 months; during the greater part of the time she had cholera on board. On putting to sea, the flies were in great force; but after a time the flies gradually disappeared and the epidemic slowly subsided. On going into Malta harbor, but without communicating with the shore, the flies returned in greater force, and the cholera also with increased violence. After more cruising at sea, the flies disappeared gradually with the subsidence of the disease."

Flügge (Die Mikroorganism, 1886, pp. 359 and 370) expresses his belief that insects may infect the food in cholera times. These numbers vary extraordinarily at times and in certain places. They must play an important role, especially when they are numerous. "A quantitative determination of this influence is of course impossible." Flügge also draws attention to the fact that the worst cholera months are those in which insects abound.

Experiments.

The first recorded experiments on insects are those of Maddox[73] (1885), in which flies (*Musca vomitoria* and *Eristalis tenax*), bees, a wasp and a beetle were fed on impure and pure cultures of the cholera spirillum, which were added to sugar. Maddox was evidently not accustomed to bacteriological methods, and gives a lengthy but unsatisfactory account of his experiments, which do not seem to have attracted any particular attention, for I only found them mentioned in the Indian Med. Gazette for April, 1886. He, however, does seem to have determined microscopically the presence of motile cholera spirilla in the dejections of the insects named, and, from his observations, concludes that insects may serve as agents in the spread of cholera.

The first to make accurate experimental observations on the rôle of flies in the spread of cholera were Tizzoni and Cattani[75] (1886) in Bologna. In two out of three experiments made with flies caught in the cholera wards and put aside for some hours, the cultures showed characteristic cultures of the cholera spirillum. Sawtchenko[76] (1892) fed flies with bouillon cultures of the cholera spirillum and found the spirilla in the flies' dejections already after 2 hours, of course in impure culture. When the flies had fed for some time on cholera culture almost no other bacteria could be isolated from their dejections. He gained the impression that the spirilla multiplied (?) in the fly's body. Previous to making cultures from the flies Sawtchenko disinfected them outwardly by placing them in alcohol and afterwards in 5 per cent carbolic. They were dried on filter paper and then cut open. He found that the *Vibrio Metschnikovi* retained its virulence after passing through the alimentary canal of the fly. Simmonds[77] (1892), working at the Old General Hospital in Hamburg, studied the flies which were present in the post-mortem room where many bodies and intes-

tines of persons dead of cholera were lying about. Catching a fly he was able to isolate cholera spirilla from it in large numbers. Thinking the many flies present might be a source of danger, he caused the bodies to be sewed up and the tables to be washed off as promptly as possible, with the result that now the spirilla could no longer be obtained from the flies in the room. As the spirilla would die from drying when attached to the outer surface of flies that are flying about, Simmonds tried to determine how long they would remain alive in this situation. For this purpose he placed flies on a fresh cholera intestine and then transferred them singly to large flasks in which they could fly and move about freely. Roll cultures made at various intervals (5 to 45 minutes) all gave positive results. In a second experiment 6 flies were placed in a bell-jar with cholera intestine and then removed to a large flask, where they remained flying and creeping about for an hour and a half. Cultures made from these flies yielded innumerable colonies. Simmonds concludes that the flies could play a serious rôle in spreading the infection, and, as a practical outcome, urges the necessity of covering cholera dejections until disinfected and of protecting food from flies. Uffelmann[78] (1892) allowed 2 flies to feed on liquefied gelatine cultures of cholera, and after they had been kept an hour and two hours respectively in a glass, he made roll cultures with them. The first yielded 10,500, the second only 25 colonies. He placed a fly similarly infected with cholera in a glass containing sterilized milk which he allowed it to drink. As soon as this had occurred, he shook the milk and made cultures from it, having first maintained it for 16 hours at 20 to 21° C. At the end of that time 1 drop of milk yielded 100 colonies of the cholera spirillum. A similar experiment, wherein an infected fly was placed on meat, gave the same result. Flügge[79] (1893), citing the experiments of Sawtchenko and Uffelmann, draws attention to the danger particularly in small households where there is no adequate separation between the cholera patient and the kitchen or place where food is kept. Especially in the latter part of summer and autumn flies simply swarm in such dwellings, and they must play an important part in spreading the infection. Macrae[81] (1894) in India, aided by Haffkine and Simpson, exposed boiled milk in different parts of the jail at Gaya where cholera and flies prevailed. A high wall separated the male from the female department and this appears to have cut off the possibility of fly infection, for no cases of

cholera occurred on the female side. The milk exposed on the male side became infected with the cholera germ, and it is certain that flies were the agents. Even the milk placed in the cow-shed and cow-shed latrines became infected, though there were no cases of cholera in that portion of the jail. The flies swarmed at Gaya in spite of disinfectants and settled in great numbers on the cholera stools, thence they gained access to the rice and milk. Macrae considers that the agency of flies will at times explain the erratic behavior of cholera, and that it "should be considered as one of the most important agencies in the diffusion of the disease." Buchanan[83] (1897) describes a jail epidemic which occurred at Burdwan in June, 1896. There were great swarms of flies that year. Outside of the prison were some huts where cholera prevailed. A strong wind blew quantities of flies from the side where these huts lay, into the prison enclosure, where they settled on the food of the prisoners. *Only those prisoners who were fed at the jail enclosure nearest the huts acquired cholera,* whilst all the others remained healthy. Though Buchanan's observation was not experimental, I think it deserves particular attention, and naturally takes its place immediately after a description of Macrae's researches. These experiments perhaps gain in value from the fact that the various investigators seem to have been ignorant of the work done by others. Only Uffelmann refers to any one else, *i. e.* to Simmonds.

The body of evidence here presented as to the rôle of flies in the diffusion of cholera is, I believe, absolutely convincing. It has not yet been determined how long they harbor the cholera germ after they have been infected, but that is, after all, of secondary interest.[1]

Typhoid Fever.

The evidence regarding the rôle of flies in typhoid fever has not been worked out as it has been for cholera. Celli[111] (1888) fed

[1] Sibthorpe[82] (1896) claimed that the flies fulfill the office of *scavengers,* destroying rather than conveying the poison of cholera. He relates that an outbreak of cholera occurred in a native regiment in India under his command. On each occasion of their leaving and occupying a new one, a recrudescence of the disease occurred. He attributes this to the flies having been left behind. Francis[80] (1893) cites the case of a woman he saw at Nusserabad in 1846, who developed cholera a few minutes after swallowing a fly and died the same evening. The title of his communication reads (!) "Cholera caused by a fly?"

flies with pure cultures of the *Bacillus typhi abdominalis* and examined their contents and dejections microscopically and culturally. Inoculations on animals were also made, proving that the bacilli which passed through flies were virulent. He made similar observations with the *Spirillum Finkler-Prior.*

Veeder[133] (1898), writing on flies as spreaders of disease in camps, says that he had once seen typhoid dejections emptied from a commode, and the latter, without being disinfected, placed near a pitcher of milk which had just been left at the door. This occurred in an otherwise cleanly household. Flies gathered about the milk and the commode and might have flown from one to the other. Veeder asks: "Is it strange that there were numerous cases of the disease in that house and others in the house next to it?" He had recently observed the behavior of flies in a military camp. He had "seen fæcal matter in shallow trenches open to the air, with the merest apology for disinfection, and only lightly covered with earth at intervals of a day or two. In sultry weather this material, fresh from the bowel and in its most dangerous condition, was covered by myriads of flies, and at a short distance there was a tent, equally open to the air, for dining and cooking (!). To say that the flies were busy traveling back and forth between these two places is putting it mildly." (He states he made cultures from the fly-tracks and excrements but does not say what organisms he found.) He concludes that the conveyance of typhoid infection "in the manner indicated is the chief factor in decimating the army." He very rightly adds: "Certainly, so far as it is known to the writer, nothing adequate has been said about it in current discussions." On the other hand, the water-supply has constantly been blamed.

It is safe to assume that the experience gathered in connection with cholera also applies to typhoid fever. Such a condition as Veeder describes when permitted by the medical authorities in charge of a camp amounts to nothing short of criminal negligence.

Tuberculosis.

Dissemination of the bacillus tuberculosis by flies.

The belief that flies (*Musca domestica*) which have fed on tubercular sputum may serve as carriers and disseminators of the

tubercle bacillus first led Spillman and Haushalter[109] (1887) to investigate the problem. They examined such flies and also their excreta deposited on the walls and windows of a hospital ward, and were able to determine microscopically the presence of large numbers of tubercle bacilli both in the intestines of the flies and their excrements. Hofmann[110] (1888), wishing to control these observations, examined the intestinal contents of house-flies caught in the room of a phthisical patient who had just died. His sputum had contained many tubercle bacilli. He found tubercle bacilli in 4 out of 6 flies examined, and also in the excreta of flies scraped from the walls, door, and furniture of the room. Flies fed artificially with sputum died in a few days. Within 24 hours of their being fed on sputum, the tubercle bacilli appeared in their excreta. He inoculated 3 guinea-pigs with the intestines of flies; one of these developed tuberculosis. Two inoculated with dry excreta remained healthy. He believed the tubercle bacilli may become attenuated in passing through the digestive tract of the fly. (He does not seem to think that he may have injured the tubercle bacilli contained in the intestine of the fly by rinsing these in sublimate before using them for his inoculations. There is nothing said as to the possible influence of light or time on the bacilli in the excreta. The question is consequently undetermined.) Celli[111] (1888), reporting experiments made under his direction by Alessi, states that the latter fed flies with tubercular sputum. Two rabbits, inoculated into the anterior chamber of the eye with the dejections of these flies, developed tuberculosis.

Observations on *Cimex lectularius* in Connection with Tuberculosis.

Dewèvre[117] (1892) collected bed-bugs in the bed of a phthisical patient. Filth prevailed, the floors soiled with sputum not having been cleaned for months. Three guinea-pigs inoculated with the contents of 30 bugs developed tuberculosis. He also crushed 50 other bugs and obtained (how not stated) virulent cultures of the tubercle bacillus from them. Microscopic examination and cultures (no details whatever) showed 60 per cent to contain bacilli. He placed bugs from another source with sputum, and was able to obtain bacilli (living?) from them weeks later. He thinks the bacilli may be parasitic on bugs (?). He thinks bugs infect them-

selves when sucking blood (?), or through sputum and soiled linen of the sick; also, possibly, the bacilli pass from one insect to another (?), thus being maintained alive for months (?) after the patient has left the room. He considers it possible that bugs thus infected may induce tuberculosis by their bites (?) especially when these are numerous. This is a gratuitous assumption upon which he elaborates at length. (The interrogation marks are mine.) Dewèvre's conclusions cannot be taken seriously.

Leprosy.

It appears that Linnaeus and Rolander considered that *Chlorops* (*Musca*) *leprae* was able to cause leprosy by its bite (Blanchard, Zool. med., II, p. 497), and Corredor (Revista méd. de Bogotà, reviewed by Polakowsky in Deutsche med. Wochschr., 30 Sept., 1897, p. 646) tells of flies in connection with leprosy, citing the case of an Indian who had lived some time with lepers and acquired leprosy, as he himself claimed, through the agency of flies. The insects gathered frequently in great numbers on the ulcers of his leprous comrades, and some of these had bitten him. The first leprous ulcers appeared on the places where the insects had inflicted wounds.

Joly[137] (1898, pp. 67-70) says his teacher, Sabrazés, has long held the view that leprosy might be produced by a large number of small inoculations, such as insects, especially parasites, may inflict. This, he considers, seems quite probable, because of the large number of Lepra bacilli which are present in the skin and ulcers in cases of cutaneous leprosy. Insects could scarcely avoid taking up the bacilli when sucking the blood or the exudations from the ulcers of leprous subjects, and might transfer and inoculate the germ into healthy individuals. He seems inclined to attribute a part of the leprosy which prevails, especially amongst the poor and unclean classes, to the agency of cutaneous parasites which are often found amongst them. An observation of Boeck's of the presence of *Sarcoptes scabiei* in a case of cutaneous leprosy led Joly to conclude that these parasites might at times serve as carriers of the infection. It appears that these parasites are very frequently found in Norway, in places where much leprosy exists; they, as also *Pediculi*, are usually present amongst the poorer classes in Algeria, which furnish the greater number of lepers. In

Soudan the *Sarcoptes* occur on almost all the dogs and often attack the natives, amongst whom there are numerous lepers. It seems to me that the possibility of this mode of transfer cannot be denied, and it is also conceivable that the pathological changes produced in the skin by the parasites may even favor the multiplication of the Lepra bacilli. Finally, Sommer[136] (1898) of Buenos Ayres, expresses the belief that mosquitoes probably act as active agents in the spread of leprosy in warm countries, but this is very unlikely.

Framboesia.

Alibert ("Maladies de la peau," p. 164, quoted by Budd[33], 1863) writes: It has been assured that the contagion of Frambœsia is greatly facilitated by a species of fly called the Frambœsia fly, which is very abundant in hot countries. The flies are constantly attracted to the sores and then inoculate the virus into healthy individuals whose blood they suck. Wilson (Diseases of the Skin, Philadelphia, 1868, p. 466) says the belief prevails in the West Indies that the disease is conveyed from one individual to another by flies. Hirsch[128] (1896) reports two cases in which he thinks the disease was conveyed by flies. Both patients were living among Fijian children who had the disease. The one had an uncovered ulcer, the other sores on his feet; "thus each had raw surfaces which could be inoculated by the poison," and would naturally be sought by flies. Cadet[134] (1897) says that lesions of the skin (ulcers, insects or leech-bites, scratches, etc.) are necessary for infection to take place. This may occur through direct contact, through infected clothes or flies, the latter transporting the virus on their feet, which are soiled with diseased secretions.

Bouton de Biskra.

That flies conveyed this disease was first claimed by Seriziat[97] (1875), subsequently by Laveran[99] (1880). Tscherepkin[98] (1876), who describes a similar affection as occurring at Taschkent, also says it is there attributed to the bite of certain insects, whence the name of the disease, "Päschä-Chûrdj," meaning "fly-bite." Seriziat claimed that a lesion of the skin was always necessary, and that the affection unquestionably resulted at times in consequence of a mosquito-bite. Laveran says that from September to October

inclusive (at Biskra), the slightest wound tends to become transformed into the bouton. He has seen it "graft itself, so to speak, on pustules of acne or impetigo, on wounds following burns or the application of vesicatories, finally on vaccine pustules." Fleming (Brit. Army Med. Rep. for 1868, X, and 1869, XI), Weber (Rec. mém. méd. mil., 1876) and Murray (Brit. Med. Journ., 1883) proved that the disease was inoculable from man to man. Laveran states that it spreads by scratching in an individual affected. He does not doubt that flies carry the virus on their feet and proboscides and thus give rise to infection.

Egyptian Ophthalmia and Florida "Sore-eye."

It has for a very long time been considered certain that flies spread Egyptian ophthalmia, and this fact has been mentioned by various authors. Budd[33] (1863) speaks of it as an established fact. Laveran[99] (1880) says it is very common at Biskra, where, in the hot season, almost all the indigenous children have their eyelids covered with flies, to which they have learned to submit, so that they do not even attempt to drive them off. The flies are constantly moving hither and thither, and carry the purulent discharge on proboscides and legs, depositing it on healthy eyes. The same has repeatedly been told me by persons who have traveled in Egypt.

In 1895, Schwarz[123 124], at a meeting of the Entomological Society of Washington,[1] exhibited specimens of *Hippelates pusio*, a small fly of the family *Oscinidae*, which swarms in great numbers in many of the Southern States, almost solely in regions which have a sandy soil. "It is particularly abundant in Florida, and is annoying to man and animals, from the fact that it is attracted to the eyes and to the natural openings of the body as well as sores." The possibility of this insect carrying disease germs was dwelt on by Schwarz, Stiles and Riley, who referred to the rôle attributed to flies in the transmission of Egyptian ophthalmia. Hubbard said that in Florida a serious disease of the eyelid is often prevalent. It is known as "sore-eye," and it becomes absolutely epidemic from time to time. He feels certain that this *Hippelates* carries the disease, since it is well known that even the use of the same handkerchief will convey the disease

[1] I am indebted to Dr. C. W. Stiles for drawing my attention to this publication.

from a sore-eyed person to a healthy one. He has known it to start with a single individual and run through an entire school or community, and thinks that *Hippelates* alone accounts for the rapid spread. Moreover, the irritation caused by the fly greatly aggravates the disease, which becomes very serious, the patient seldom recovering entirely from it, but being affected by weak eyes ever afterwards." This fly is vulgarly termed "gnat," and it is not able to "bite."

Favus, Impetigo, etc., and Pediculi.

Dewèvre[117] (1892) claims that pediculi disseminate impetigo. He removed ten pediculi from a child suffering from impetigo and placed them on a healthy infant, which a few days later developed impetigo. The experiment was repeated several times with the same result. In a second series of experiments, he took scrapings from under the nails of children that had impetigo, and, placing them on artificially scratched places, reproduced the disease. Lastly, he took pediculi from a child that was not affected with impetigo and placed them on a child that had the disease. Removing them after twenty minutes, he placed them on a healthy child. The latter acquired the disease, as did 50 per cent of the children so experimented upon. He claims the specific micro-organism adheres to the front legs especially, as also to the hairs of the insect, and the latter carries them about as bees do pollen. In the last set of experiments, he only allowed the pediculi to remain half an hour on the healthy head, but this was sufficient to produce infection.

Aubert[100] (1879) considered pediculi caused impetigo, prurigo, pityriasis, etc., "ils prédisposent à la contagion et à la généralization des teignes," this being especially true for favus, "dont les spores trouvent, dans le suintement ou les croûtes d'un impétigo, des conditions favorable de fixation et d'adhérence."

Miscellaneous.

Thomas Sydenham (1624-1689. Sydenham's Works, Sydenh. Soc., Ed. I, 271, cited by Davidson[309], 1898) remarked that if swarms of insects, especially house-flies, were abundant in summer, the succeeding autumn was unhealthy.

Crawford[89, 90] (1808 and 1811) calls attention in a general way to the rôle which insects and lower forms of animal life may play in transferring disease.[1]

Holscher (1843), of Hannover, as also his predecessor (cited by Marpmann[129], 1897), claimed that flies played a great rôle in epidemic diseases, he having frequently convinced himself that in years when flies were numerous no epidemics or only mild epidemics occurred. This is just the reverse of the opinion usually held.

In the Lancet for 1863[87] occurs the statement: "The inhabitants in the neighborhood of the cemetery of Montmartre, Paris, have suffered from attacks of a 'gangrenous fly,' which causes inflammation, mortification and death within 24 hours. Many persons have fallen victims." In the same journal for 1867 (Vol. II, p. 28, July 6th) it is stated that "a swarm of poisonous flies has appeared in Transylvania, and have killed, it is said, more than 100 head of cattle. Beasts are kept shut up; large fires are made. Tobacco smoking is found to be the best preventive as regards human beings."

Leidy[94] (1872), speaking at a meeting of the Philadelphia Academy of Sciences, expressed the belief that flies might spread all contagious diseases, and referred especially to them in relation to hospital gangrene. He had had occasion to observe a fly feeding on the juices of *Phallus impudicus*. On catching the fly by the wings, he found the spores of *Phallus* in the drop of fluid the insect extruded from its proboscis. The spores were also found in the stomach of the fly. He concluded from this observation that flies could also act as carriers of the virus of wound infection.[2]

Gerlach[95] (1873, p. 48) states that fly-maggots very soon digested trichinæ contained in meat on which they were fed. Already, after a few hours, no trichinæ were to be found. Cloos, Davaine, Pagenstecher and Fuchs had also obtained negative results from feeding frogs, water-salamanders, earthworms, fly-maggots, and beetles (both land- and predatory aquatic beetles) with trichinæ.

[1] I am indebted for this reference to the kindness of my friend Prof. William S. Thayer of Baltimore.

[2] Sir John Lubbock[93] in 1873 provoked a laugh in the House of Commons by the following remarkable extract from one of the books used in the elementary schools: "The fly keeps the warm air pure and wholesome by its swift and zigzag flight." (!)

Probstmayer had likewise, prior to Gerlach, seen that trichinæ were digested by maggots.[1]

Cobbold[253] (1879) considers that insects may carry the eggs of the fluke which they have ingested and transport these to water, thus contaminating it. This might explain how *Fasciola hepatica* and *Planorbis marginata* become infected.

Referring to the rôle of biting insects in the spread of infection, King[273] (1893) wrote: "Furthermore, when it is remembered that disease-producing bacterial germs are so minute that a million may rest on the head of a pin, and that the smallest puncture of the finest needle-point (as in Pasteur's experiments with chicken-cholera), when charged with an atom of infecting matter, may be sufficient to infect the body with the septic matter, it scarcely seems possible to ignore any longer the punctures of mosquitoes and other proboscidian insects as possible sources of both infection and contagion."

Grassi[104] (1883) concludes from his observations on flies that they play a great rôle in the spread of infectious diseases. In some countries flies are active during half the year, in others the whole year round. He believes that they spread infection by feeding on tubercular sputum or on typhoid stools, and that they are also responsible for the spread of favus, silkworm disease ("flacherie") and foul brood among bees.

Grassi broke up segments of *Taenia solium* in water, the same having been preserved some months in alcohol. The flies came and sucked up the eggs with the water. The eggs came away unaltered in the insects' dejections. The same thing was observed to occur with the eggs of *Oxyuris*. Experimenting with unsegmented eggs of *Trichocephalus*, which were placed on the laboratory table at Rovellasca, he saw the flies feed on them, and, some hours later found the eggs in the dejections of the flies, which had been deposited in the kitchen in the story beneath, at a distance of 10 meters from the place where the insects had been fed. He placed sheets of white paper in the kitchen on which the flies defecated, and he also caught some flies there whose intestines were full of the eggs. That flies are able to take up corpuscular elements through their proboscides was thus proved. He also fed them on *Lycopodium* spores, *Oïdium lactis* from cream, and the spores

[1] Dr. C. W. Stiles kindly drew my attention to this publication.

of *Botrytis* taken from silkworms. Both the *Oïdium* and *Botrytis* were found in the flies' dejections. He considers that even if it were proved that flies digest pathogenic bacteria, they could not be relied upon to do so, for they often pass *undigested* food, and, besides, may carry them about on their feet, etc. The vehicles, air, water and soil do not account for all cases of diffusion of disease; many cases may be due to the agency of insects. Consequently, Grassi recommends that flies be destroyed as far as possible, perhaps using our knowledge of their diseases for their destruction.

Stiles (1889 or 1890—personal communication) placed the larvæ of *Musca* with female *Ascaris lumbricoides*, which they devoured, together with the eggs they contained. The larvae, grubs, as also the adult flies, contained the eggs of *Ascaris*. The experiment being made in very hot weather, the ascaris eggs developed rapidly and were found in different stages in the insects, thus proving that the latter may serve as disseminators of the parasite. Providing that the eggs attain the proper stage of development, the fly, acting simply as a carrier, might convey the parasite to man by falling into or depositing its excreta on food.

von Nordenskiöld (1883, loc. cit.) attributes the bad effects of the bites of gnats in Greenland to these insects having previously fed on the refuse about the colonies, where there was always a good deal of decaying animal matter containing "Bakterienheerde mannichfacher art." He adds that if one is once severely bitten by these insects almost complete protection against the poison appears to result.

Flügge[107] (1886) refers to insects as possible carriers of infection when they have soiled themselves with the fresh or dried excreta of the sick. Celli[111] (1888) states that medical as well as popular experience had shown that erysipelas and anthrax may be transmitted by the bites of insects. He reported experiments which showed that the *Bacillus anthracis*, *B. typhi abdominalis*, *Spirillum Finkler-Prior* and *Staphylococcus pyogenes aureus* still retained their virulence after passing through the fly's intestine, and suggested various measures to be taken against flies.

Flügge[112] (1891) considers biting insects of probable importance in the spread of such infectious diseases where infection occurs through the entrance of germs directly into the blood. He thinks vermin may play a rôle this way in *Febris recurrens*, and mos-

quitoes in malaria. Ordinary flies (*Musca domestica* and the like which do not bite) may carry the agents of infection from diseased to healthy individuals directly or contaminate the food, thus giving rise to disease. Insects are to be regarded as important agents, because they may carry a concentrated virus, the latter being usually diluted when air or water acts as a vehicle. Correa[121] (1892), in an article of a general character, which contains no original matter, cites almost all the infectious diseases as probably being transmittable through flies. Moore[122] (1893) states that in his book on "Health in the Tropics," published in 1853, he drew attention to the necessity of guarding food against flies. He also thought mange transmittable through insects. (See "Selections from the Records of the Government of India, Foreign Department, No. 108," and "Marwar, the Land of Death," Indian Annals of Med. Sc., 1876). He thinks flies may also spread cholera, typhoid, tuberculosis, anthrax and leprosy. He remarks: "Flies in the East have not far to pass from diseased evacuations or from articles stained with such excreta, to food, cooked and uncooked."

Morau[125] (1895), who observed a tumor in the axilla of a white mouse in his laboratory, extirpated the growth, which proved on examination to be an "epithelioma cylindrique." A half of it was broken up and a suspension of it injected subcutaneously into mice. The result was that all these mice developed similar tumors. Morau states that the descendants of these infected mice showed themselves to be more susceptible than others by the rapidity of the malignant growth. Mice in advanced stages of the disease were assailed by large numbers of fleas, lice and bugs. Morau thought these might play a rôle in the spread of the disease, so he made experiments which were intended to prove this. He placed mice in infected cages, to which he added many bugs. Control mice were placed in new cages which were insulated by being placed with their supports resting in saucers containing turpentine and camphor. After some months all the control mice were healthy, the others diseased. Morau says that since then he has often used bugs instead of the syringe for inoculating the animals. Inoculations on rats, guinea-pigs and rabbits gave a negative result, whilst 4 out of 10 Algerian rats were successfully infected. These statements certainly require confirmation before they can be accepted, the superficial manner in which they are made argues against their accuracy.

Laveran[287] (1896) cites a number of affections (mentioned above) in which various observers have shown more or less conclusively that insects may act as carriers of infection. Marpmann[129] (1897) makes a few general remarks on the subject, whilst Bosc[130] (1897) theorizes very freely. He has found gregarines in almost all the insects examined in central France, and it is easy, he claims, to understand how these may infect fish, rabbits and snails, etc. He believes that insects play an important rôle in cancer, a disease which he says is more frequent in the country, where insects are also more numerous. He cites a case told him by Prof. Forgue of a woman who was bitten on the cheek by a fly which she struck and crushed at the spot where it had bitten. Shortly afterwards an epithelioma appeared and developed rapidly at the place where the insect had bitten her. He believes there is particular danger in crushing insects on the skin, for gregarian cysts are thus liberated and may give rise to infection. Biting insects, such as mosquitoes, may infect their proboscides with protozoan parasites by drinking stagnant water, and thus convey infection whilst sucking blood. He thinks this is what happens in malaria.

Ashmead[127] (1896) thinks ichneumon flies of the subfamily *Ophionidae* may produce infection, "since these insects are attracted to decaying animal and vegetable matter and might have carried bacteria to the patient which caused blood-poisoning."

In an editorial note in Janus (1898, p. 97) the remark occurs that the belief in the relation of flies to the spread of infectious diseases is a matter of tradition and general belief, mention of the rôle of flies being found throughout medical literature. It used to be a saying amongst the people in Holland "een vliegenjaar een Ziekenjaar."

Joly[137] (1898), in his thesis, dwells on the rôle of insects in the fertilization of plants. Insects may carry about dust moulds and bacteria on their hairs. He had seen how mould developed about flies which had accidentally fallen into his paste-pot. In the same way they may also transport bacteria, and, if coprophagous, may carry disease germs and deposit them on food and in dwellings. He cites a few affections which might originate from insects acting thus as passive agents. A *Tabanus* (species?) caught by him on a heifer near the municipal vaccine station yielded colonies of *Staphylococcus pyogenes aureus* and *albus*, a *Streptococcus*, and a

Streptothrix. A house-fly caught in the clinical laboratory yielded *Staphylococci* and a short motile pathogenic bacillus, and three others caught near a rag shop were shown to be carriers of a pathogenic cocco-bacillus. Joly also describes how flies may transport germs within their alimentary canals and spread disease by means of their excreta, and describes how biting insects may serve as active agents in the dissemination of the disease. He states (p. 17) that it is a common belief in Guadaloupe that glanders is transmitted (" passively ") by flies, which are very numerous there, and considers that this mode of infection may also occur at times in Europe. I might add here that Osborn[338] (1896, p. 122) says *Stomoxys calcitrans* Lin. has been blamed as transporting and inoculating glanders in horses.

Ixodidae.

Various members of this family have been accused of propagating infectious diseases. We shall refer separately to the rôle of *Ixodes bovis* (Riley, 1869) or *Boöphilus bovis* (Curtis, 1890) in Texas fever. In the case of the other *Ixodidae*, it has not been shown that they convey disease from sick to healthy animals, and it would appear as if the infections which follow their attacks were the exception and not the rule. It seems to me as if in a number of cases the lowered resistance of the part, produced by the effects of the bite, favored a subsequent bacterial infection.

Ixodes ricinus is reported by Dulbreuilh (1838) as causing and being contained in a pustule situated in the mastoid region. He cites several cases of phlegmonous inflammation following their bites in man. Various pathogenic effects due to this tick are referred to by Desprès[145] (1867) and Liégois. Mauvezin (cited by Railliet[212], 1895) says that its bite may cause gangrenous inflammation in sheep, whilst in man the bite may be followed by abscess, œdema, congestion of the lymphatic glands, lymphangitis, chills, fever, etc. Allan[151] (1881) writes that he was bitten in the axilla by a tick (species?) which penetrated deep into his skin before he tore it out. The next day he suffered from malaise, headache, loss of appetite, thirst, œdema, stiffness in the arm and shoulder, the axillary glands being much swollen and painful. A pustule formed at the seat of the bite, the center of which became

necrotic, etc. Johannesen[157] (1885) describes the case of a boy who was attacked by an *I. ricinus* whilst resting in a wood. The body was torn from the head of the tick; the head not being removed remained imbedded in the skin on one side at the back of his head. Swelling followed at this point, and there followed symptoms of headache, stiffness and cramp in the muscles of that side, polyuria, partial loss of memory, the pupils being widely dilated, etc., the boy making a slow recovery. Johannesen cites a case reported by Vogt (1869, in "Nedeüas Amt") as occurring in Norway, where a tick's bite caused œdema of the perinæum, scrotum and penis, accompanied by retention of urine. It appears that in Norway great stress is laid on not tearing off the head of a tick that has begun to bore itself into the skin, the use of butter, oil or turpentine being recommended (as elsewhere) for the purpose of making the tick drop off. All who are familiar with ticks will, I think, give similar advice. Railliet cites Ronsisvalle as reporting that *Hyalonema aegypticum* (L.) may cause grave local effects in man, which he attributes to a venom, whilst Railliet believes that the effects are to be ascribed to the entrance of pathogenic germs into the wound. Blanchard (Zoöl. méd., 1890, II, pp. 326, 334) considers that ticks may carry the bacilli of tetanus and anthrax into the wounds they inflict, but he does not back the statement (which seems to me doubtful) by facts.[1] Railliet[243] (1895, p. 711) cites Couzin as stating that in Guadaloupe ticks are considered to play an important rôle in the spread of a disease there which they call glanders ("farcin"), and Railliet thinks they may inoculate a specific micro-organism. Williams (1895) removed ticks from sheep affected with "louping ill," and placed them on healthy animals. The result was negative, as were also those of inoculations with "the organism" (?) taken from ticks. Only quite young ticks adhered to the animals to which they had been transferred. The records of Williams's experiments are quite unsatisfactory. Meek and Greig Smith (Veterinarian, 1897) consider that ticks inoculate (?) two pathogenic germs, the one being a pyogenic organism, the other a bacillus. They state that the latter produces symptoms similar to those of "louping ill." No

[1] Blanchard cites Chillida (1883) and Raymondaud (1884) in this connection.

conclusions as to the rôle of ticks in "louping ill" can be formed from the work here cited.[1]

The bite of different species of the genus *Argas* is frequently followed by pathogenic effects which some authors attribute to the action of a poison secreted by the argas, others to the inoculation of infectious organisms. In their habits these blood-suckers may be said to resemble bed-bugs, for which they have not infrequently been taken. They seem to be most active at night.

Argas reflexus, which is found in pigeon-houses, occurs in Italy, France, Germany, England and the United States (Railliet[242], 1895, Osborn[338], 1896, Brandes[159], 1897), the larvæ being vulgarly termed pigeon-lice. When numerous they may cause the death of pigeons, and have been observed to wander into chicken-houses and dwellings. They do not seem to annoy chickens, but they occasionally attack man and cause much trouble. Raspail (1838) attributed an eruption on a child's neck to the bites of this species, but Railliet thinks he was wrong in doing so. Boschulte[144] (1860) describes the case of a family, several members of which were bitten by *A. reflexus*, only pain and slight swelling following in all cases excepting that of an old man. The latter was bitten on the lower part of the thigh, with the result that a deep, circular suppurating wound about the size of the head of a pin marked the spot where he had been bitten. There was extensive œdematous swelling and redness of the surrounding parts. Boschulte allowed himself to be bitten by an argas. It took 27 minutes to fill itself with blood, and then dropped off. The pain was like that of a mosquito-bite. A small drop of coagulated blood subsequently covered the puncture. Nothing especial was noticed, and three days later the wound had healed. Ten days after he had been bitten the spot began to itch and showed a nodular swelling, which grew red and increased to the size of a pock. No exudation of serum occurred, but the itching was very annoying. This subsided after six days, a small scab was cast off at the point bitten, and the skin resumed its normal appearance. Boschulte[140] (1879) reported, nearly twenty years later, that the place where he had

[1] I am indebted to Mr. Thomas Bowhill of Edinburgh for abstracts of these publications on "louping ill" to which he kindly also drew my attention. See Williams, Princ. and Pract. of Vet. Med., 1897, p. 568, "Louping Ill. Further researches into the causation and prevention of louping ill, or tumbling, in sheep. Ixodic toxæmia."

been bitten still showed a sharply-defined circular flattened elevation with a central cicatrix, and that in the interim several similar, but smaller elevations had appeared in its vicinity. Taschenberg[118] (1873) wrote that *A. reflexus* attacked some children in Friedeburg, biting them especially on the hands and feet during the night. The itching pain from the bites traveled upwards to the shoulders and hips and lasted about a week. Chatelin (1882, cited by Railliet[242], 1895, p. 717) reports the case of a child that was bitten by *A. reflexus* which had wandered from the pigeon-house into the dwelling. The pigeon-house had not been used for years. The bites were followed by pain and œdematous swelling, which persisted for some time. Other persons who were bitten at the same time exhibited no such symptoms. Alt[158] (1892) saw a case which occurred under similar circumstances, where the bite was followed by urticaria factitia and general erythema, which subsided in a few hours. Brandes[159] (1897) also describes this case—that of a man who had been bitten five times in four years. Hauch, who attended him, stated that he woke at night with pain about the wrist, on which he discovered the argas. Within half an hour an erysipeloid swelling spread from point of the puncture all over the body, increasing, particularly about the head, until the eyes were hidden by the swollen lids. During this time the patient suffered from shortness of breath, palpitation, dullness, etc., for an hour, when the symptoms began to subside with the appearance of profuse perspiration. The swelling gradually subsided during the following 10 to 15 hours. The patient, who seems to have been peculiarly susceptible to the bite of the argas, had previously kept pigeons in his house, but the pigeon-house had been walled up two years before.[1] As Brandes states, this latter proceeding seems to have caused the migration of the parasites into the dwelling. Alt[158] (1892), and two other persons, allowed themselves to be bitten by *Argas reflexus* obtained from the abandoned pigeon-house. The parasites took about twenty minutes in which to fill themselves with blood. Slight pain, that came and went, followed, but nothing in particular occurred, excepting in one case,

[1] *Argas reflexus* is able to live a long time without food. Hermann saw them survive 8 months, Railliet 14 months, Ghiliani 22 months (Railliet, 1895, p. 717). Brandes states that living specimens were found in the abandoned pigeon-house referred to after the lapse of two years.

where, after four to five days, a painful nodule, the size of a pea, appeared at the seat of the puncture, but this disappeared soon afterwards. Two persons who suffered from urticaria also allowed themselves to be bitten; one of them remained unaffected, whilst the other developed general erythema after four hours, which subsided again in an hour. Brandes reports a case which was observed in 1884 at Oschersleben, where a man became so œdematous after four to five hours that his clothes had to be cut off. The œdema is said to have lasted three days in this case. The effects here noted seem to depend on a peculiar idiosyncrasy. Brandes believes that a poison is probably elaborated in the salivary glands of *Argas*. Alt, who injected three of them, which had been crushed, subcutaneously into a dog, produced symptoms of intoxication in the latter which were similar to those which are produced by small quantities of viper ("Puffotter") venom.

Argas persicus, Fischer, the "Garib-Guez" of the Persians, also known as the "punaise de Miana" (Miané or Mianeh), has a rather formidable reputation. Dupré[139] (1809) seems to have been the first to write regarding it, stating that its bite is at times dangerous, causing prolonged sickness. Kotzebue[140] (1819) says that it behaves like a bed-bug, and may so infest villages as to drive out the inhabitants. The natives, he relates, are comparatively immune, but foreigners suffer severe pain, delirium and convulsions, and even death, within 24 hours in consequence of its bite. Fischer de Waldheim[141] (1823) also says that the bite of this species may prove fatal. Heller[145] (1858), who examined their anatomy, denies that they have a poison gland, and ascribes the effects to the mechanical injury (!) done by the parasite. Taschenberg[146] (1873) thinks that the effects ascribed to *Argas persicus* are really due to a fever which prevails in Miana ("dem in Miana herrschenden Faulfieber"). Schlimmer[147] (1874), of Teheran, considers that the relative immunity of the natives is acquired by their having been bitten at some time or other by the *Argas*, and that such bites act like a preventive inoculation with vaccine against smallpox. He says the symptoms are like those of "remittent fever, extreme lassitude, disinclination to work, yawning, fever, perspiration, not accompanied by much thirst, increasing and decreasing at stated hours in the day," so that many think it is only malaria acquired during a short stay at Miana. Schlimmer does

not share in this opinion, and denies that the natives are subject to malaria. He says that fatigued travelers, and those that have undergone privations, are especially susceptible. *A. persicus* is also found at Chahroudé and Bestham on the main road from Teheran to Khoragan, where it is called "Bhebguèze," which signifies "biting at night." No malaria exists in these parts, but the effects of the *Argas*-bite are the same as at Miana. Schlimmer relates that he once (1858) treated 400 soldiers who claimed to have been bitten by these parasites at Miana, but many were unable to state on what part of their body they had been bitten. The soldiers suffered from the symptoms above described, and were promptly cured by the aid of "le poudre minerale de Bondin," or, when the cases were refractory, by the administration of quinine. Bordier[154] (1882), who reprints the part of Schlimmer's publication from which the above data are quoted, inclines towards the supposition that the effects of the argas bite are due to a poison, and, referring to the reported immunity of the natives, says that this reminds him of the fact that in many countries it is the strangers who are especially attacked by mosquitoes, the natives having apparently acquired a resistance towards the poison of these insects.

Mégnin[152] (1882, p. 305) after casually stating that he had kept an *Argas* alive without food for four years, denies the statement generally made by medical zoölogists that the bite of *A. persicus* is dangerous. He refers to a letter of Tholozan's to Laboulbène which says that it is the belief among the common people in Persia that the bite of *Argas* is dangerous and fatal to foreigners, intermittent and remittent fevers being attributed to it. Fumouze repeatedly placed a female *Argas* on a rabbit's ear from which it sucked blood, but no pathogenic effects followed. Brandes (1897), in view of his experience with *A. reflexus* cited above, considers that the effects of the bite are due to a poison.

The *Argas Americanus* Packard has caused the death of chickens in Texas according to Osborn[335] (1896, p. 256), and the same is related of *A. Mauritianus* Guér., which is found on the Island of Mauritius (Railliet[242], 1895, p. 718) *Argas Tholozani* Lab. and Mégnin, the "Kené" of the Persians, the "punaise de mouton" of French authors, which seems to act like the others, is also claimed to be harmless by Mégnin[152] (1882), who allowed one to bite his hand. It sucked itself full in about half an hour, the

pain produced being less than that of a leech. The only effect was the formation of a violet ecchymosis six mm. in diameter about the bite. As Johannesen[137] (1885, p. 347) very properly remarks, one experiment by Mégnin (in France) with an *Argas* which had been kept starving for years, has no value as proving that its bite is innocuous under normal conditions. *Argas Talaje* Guerin Menneville[142] (1849), which occurs in Central America, causes intolerable itching and pain by its bite. Mégnin[156] (1885) says its saliva may be venomous like that of the mosquito or tarantula. This stands in direct contradiction to his previously expressed views regarding *A. persicus*. In Mexico, *A. turicata*, A. Dugès, may also cause serious effects by its bite. The Mexican name for it is "turicata." It has been known to kill pigs by its bites. Dugès[148] (1876) says that chickens fed on turicatas die about the third day. The effect of the bite in man is especially bad if the turicata's rostrum is torn off, and, where this occurs, Dugès recommends the use of the cautery, otherwise it causes severe itching, and an ulcer forms at the spot bitten, and this may persist for months, or there may develop erysipelatoid dermatitis, lymphangitis, the formation of bullæ containing serum about the puncture, at times gangrene, subcutaneous abscesses, etc. In three cases he reports general symptoms followed the bite. In two of these a vein had been punctured by a turicata. One patient had difficulty in speaking and swallowing, swelling and numbness spreading over the whole body, vomiting and diarrhœa. In another patient all these symptoms subsided within an hour, when an urticaria made its appearance, accompanied by profuse perspiration. Dugès says people are reported as having died from the bites of turicatas, the noxious effects of which he attributes to a venom, a peculiar idiosyncrasy existing in certain individuals. *Argas Mégnini* Dugès[148] (1883), the "garrapatas" of Mexico, Mégnin considers to be less injurious; he kept some of them alive two years without food. A list of other species of *Argas* is given by Railliet[242] (1895, pp. 717 to 718). Reclus[150] (1880) gives a rather harrowing description of the sufferings he endured from garrapatas in Central America.

I think the effects due to the bites of different species of *Argas* here described fully justify the conclusion that the acute symptoms are due to a poisonous saliva. Bacteria may of course gain

access to the wounds inflicted, which are possibly more prone to infection in consequence of the injurious influences of the secretions of the *Argas*. Depending on the character of the organisms introduced, the later symptoms will naturally vary. It is not proved that they inoculate infectious agents. In this connection it is of interest to note that Marlatt[163] (1896) describes effects somewhat similar to those which at times follow the bites of *Argas*, as occurring in persons who have been bitten by the blood-sucking cone-nose (*Conorhynchus sanguisuga* Lec.) in America. He quotes observations by Lembert in California, and Toumey in Arizona.

Sarcopsylla penetrans.

The effects produced by this parasite, which is found distributed from the north of Mexico to the south of Brazil, being also introduced into Africa about 1872, and recently into the East Indies, are sufficiently well known to make it unnecessary to enter into details. They have been described by Labat[164] (1833), Nieger[165] (1858), Haine[167] (1860), Rowell[166] (1860), Karsten[168] (1865), Brassac[169] (1865), Bonnet[170] (1867), Gage[171] (1867), de Argumosa[172] (1871), Laboulbène[173] (1874), Canoville[174] (1880), Pugliesi[175] (1888), Julien and Blanchard[176] (1889) and many others, and are mentioned in the works of Neumann[210] (1892), Railliet[242] (1895) and Blanchard[202]. The fecundated female flea penetrates the skin of its host (man, and a large number of warm-blooded animals) and remains attached there for six to seven days. During this time its abdomen swells to the size of a pea whilst the eggs are maturing. When the latter are fully developed, the flea is often expelled by the pressure of the inflamed tissues about it, and, being freed, the flea proceeds to lay her eggs. Complications, however, frequently arise in consequence of the rupture of the flea and the escape of its contents into the wound, or the entrance of pathogenic germs from without. Ulcerations, abscesses, destruction of joints, phlegmons, erysipelas, lymphangitis, etc., may follow. Karsten says that tetanus often follows the removal of the flea from the foot (the part most attacked in man), which is to be explained by the entrance of earth into the wound whilst walking. The negroes are said to be adepts in the art of removing the *Sarcopsylla* without rupturing its body.

Trombidiidæ.

A variety of cutaneous affections have been attributed to the agency of different species of *Trombididae*. Joly[137] and others regard them as passive carriers of infectious agents, but this seems to me very doubtful. It is much more probable that their irritating secretions are the cause of the effects produced by their presence on the skin. The formation of ulcers, etc., is probably due largely to secondary bacterial infection brought about by the scratching of the skin, the resistance of which may also be lowered by the presence of the acari. The following is taken chiefly from Railliet[242] (1895, p. 694 to 699):

Pediculoides ventricosus (Newport) was observed by Lagrèze-Fossot and Montané (1850) to cause severe itching on the breast, arms, face, neck and shoulders of persons handling grain which contained it. The irritation of the skin was followed by a pimply eruption with more or less inflammation. Similar observations were made with regard to other species of pediculoides in India by Rouyer and Robin (1868), in the Gironde by Perrens and Lafargue (1872), at Klausenburg by Geber (1879), in Budapest by Koller (1882), in Algeria by Bertherand (1888); in the last case the presence of *P. ventricosus* being determined by Moniez. *Tarsonemus intectus*, Karpelles (1885), was observed in Hungary to cause an affection analogous to urticaria, accompanied by intense pruritus. *Pygmephorus uncinatus* (Flemming, 1884) caused the sudden appearance of an unusual exanthematous affection in workmen at Klausenburg who were engaged in handling grain that had come from Russia. The hexapod larvæ of various species of *Trombidium* cause similar effects: *Leptus autumnalis* (Shaw), the harvest-bug, is especially abundant in the west of France, and also occurs in England and parts of Germany, where it attacks man and animals (cats, dogs, cattle, sheep, horses, chickens; it may be fatal to chicks hatched in autumn), especially smaller mammals like hares, rabbits and moles. They may pass from these animals to man by contact. According to White, some persons are more liable to be attacked than others, and different persons are variously affected. All experience intense pruritus, and a smarting pain which prevents sleep. The skin is continually scratched and this gives rise to complications, excoriated papules and an exzematoid condition. More or less extensive erythema is observed in susceptible individuals. The skin is swollen, reddened, and at times exhibits purplish discolorations about the spots where the harvest-bug has bitten. At other times there may be a papular urticaria, vesicular eruptions, and a brief but sharp rise of temperature. Other species of *Leptus* are known to produce similar effects. This is the case with the *Akamushi* in Japan, *Leptus irritans* Riley (the most frequent form in the United States and Mexico, the *Tlasahuate* in Mexico, the "pou d'Agouti" in Guyana, the "bête rouge" of Martinique, the "colorado" of Cuba, etc., etc.

In this connection see also U. S. Dept. of Agriculture, Div. of Entomol., Bulletin No. 5. Brucker[162] (1897) determined a lupus found on a man in

France to be the larva of *Trombidium gymnopterorum*. The writings of Palm[160] (1878) and Baelz and Kawakani[161] (1879) show that there is no ground for the belief that a leptus bears any relation whatever to the "Island-Insect Disease," or "Shima Mushi," in Japan.

DISEASES DUE TO ANIMAL PARASITES.

Dypilidium caninum (L.).

(Synon., *Taenia cucumerina*, Goeze; *T. elliptica*, Batsch, 1786, etc.)

The adult tape-worm is found in the dog, occasionally in the cat, rarely in man.[1] The larval stage is found in fleas and dog-lice, and these, gaining access to the alimentary canal of the warm-blooded host, give rise to infection. Leuckart[184] had supposed that an insect might harbor the larvæ, and Melnikoff[179] (1869) discovered them accidentally in the visceral cavity of the dog-louse (*Trichodectes canis*), where they occurred as small white bodies which Leuckart examined and determined to be the larvæ of *D. caninum*. Metschnikoff also observed the larvæ in the dog-louse. Subsequently, Melnikoff succeeded in infecting dog-lice by placing ripe segments of the tape-worm, which he had previously crushed, so as to liberate the eggs, on a part of the dog's skin which was infested by lice. The observation that the tape-worm was often found where lice were absent suggested that some other insect might also serve as an intermediary host, and this was shown to be the case by Grassi and Rovelli[196 197 199] (1888 to '89). These investigators found that the dog-flea (*Pulex serraticeps* P. Gerv.) more usually harbors the larvæ, but that even the flea which infests man (*P. irritans*) may be the intermediary host. Only adult fleas (never their

[1] Dubois, Salzmann, Leuckart, Krüger, Brandt, Hoffmann, Blanchard, Krabbe and Friis cite cases of the occurrence of this worm in man. The cases reported by Salzmann and Leuckart were in children aged 9 months and 3 years. Krüger[194] (1887) observed it in a 16 months' child which played about on the ground with a filthy little eczematous dog. Brandt[198] (1888) reports two cases: the first, that of a boy who became severely infected from playing much with a chained dog, although he had remarked the presence of lice on the dog and even caught them on his own person. The second case was that of a girl with a lousy, long-haired dog that slept alongside her bed. Brandt found two dog-lice on the girl's head. Krabbe[220] (1896), who collected a number of cases, showed that almost all occurred in infants a year old, the tape-worm only being found once in a child of 4 years, etc.

larvæ) contain the parasites. Neither *Haematopinus pilifer* (Burm.) nor flies serve as hosts. Sonsino[198] also found that the dog-flea is the usual host. Grassi found that the worm-embryo soon after gaining access to the insect became transformed into the larval form. As many as 50 larvæ were found in a single flea. As a rule, they are not so numerous within the body of the insect. Where there are many, the larvæ are of smaller size. If the contents of an infected flea are fed to a dog the parasites usually die, infection occurring normally when the whole insects have been swallowed. Dogs infect themselves by devouring their fleas and lice. Children may become infected from playing with and kissing dogs, their vermin being unconsciously swallowed. The worm-larvæ are liberated in the intestine through the digestion of the flea's or louse's body; they then exvaginate and take on their definite form, in a manner similar to *Taenia solium* or *T. saginata*. (See for further particulars Leuckart[184] [1876 to 1886], Grassi[196 197 199] and Sonsino[198] [1888], Railliet[242] [1895], etc.)

Drepanidotænia infundibuliformis (Goeze, 1782) Railliet, 1893.

The hosts of this tape-worm are chickens (*Gallus domesticus*), the migratory quail (*Coturnix coturnix*), the mallard and tame duck (*Anas boschas and A. b. domest.*) and sparrow (*Fringilla domestica*). The occurrence in the pheasant (*P. colchicus*), crowned pigeon (*Goura sp.*) and domestic pigeon is not certain. Grassi and Rovelli[199 208] (1889 and 1892) claim that the cysticercoid develops in the ordinary house-fly (*Musca domestica*), in which they state they found the larval parasite. They, however, give no experimental proof of their statement. Stiles[232] (1896) does not deny the possible correctness of their hypothesis that the fly is the intermediary host, but insists "that it is only a hypothesis, with little back of it, and that it is now time to call a halt on such speculative work and to distinguish between what is shown experimentally to be fact, and what might possibly be shown to be fact."

Davainea cesticellus (Mollin, 1858) R. Blanchard, 1891.

This tape-worm occurs in chickens. Grassi and Rovelli[199] (1889) believe the intermediary host to be a lepidopterous or coleopterous insect. Stiles[232] (1896) states that the development of the parasite is unknown.

Tænia serpentulus Schrank.

von Linstow[215] (1893) states that he has found this tape-worm in different places (Ratzeburg, Hameln, Göttingen), parasitic in *Corvus corone*, and that it has also been found in *Corvus cornix*, *C. frugilepus*, *C. monedula*, *Garrulus glandarius*, *Nucifraga caryocatactes*, *Pica caudata*, *Oriolus galbula*, *Picus major* and *P. aurulentus* in Germany, Austria, Denmark, Turkestan and Egypt. von Linstow (who describes, figures and gives the literature relating to this worm) claims to have found the cysticercus in a beetle, *Geotrupes sylvaticus*, which is often found on horse-dung. In beetles caught on a road near Göttingen he found numerous cysticerci in the body cavity. von Linstow seems to rely entirely on the morphological diagnosis of the parasite, and does not state that he made any infection experiments.

Tænia furcata.

Tape-worm of the shrew-mouse (*Sorex*), described by Stieda (1862) as rare, von Linstow[223] (1897) believes he found the cysticercus in the horse-dung beetle *Geotrupes sylvaticus*.

Hymenolepis pistillum (Duj.).

(Synon., *Taenia pistillum*.)

This tape-worm occurs in the shrew (*Sorex araneus*), and Villot[185] (1877) found the cysticercus in a myriapod (*Glomeris*). Villot had previously described the cysticercus as *Staphylocystis*. The ripe segments of the tape-worm, containing eggs and embryos, break off and are given off in the fæces of the shrew. The embryos then rupture their envelope and become free. The *Glomeris* devours the embryos, which bore through the intestine of their host and become lodged in the adipose tissue about the biliary vessels. The worm-embryos then lose their hooks, become vesicular and proliferate, being transformed into scolices. A shrew devouring such a myriapod introduces a hundred or so of scolices into his digestive tract, where they may give rise to as many tape-worms.

Hymenolepis diminuta (Rud.).

(Synon., *Taenia diminuta*, Rud., 1819, etc., etc.)

The adult tape-worm is found in *Mus decumanus*, *M. rattus*, *M. musculus*, *M. Alexandrinus*, and has also been observed in man. The larval stage (*Cercocystis H. diminutae* or cysticercoid of Stein) has been observed in Lepidoptera (*Asopia farinalis*, in caterpillar and butterfly), in Orthoptera (*Anisolabis annulipes*, an earwig) and in two adult Coleoptera (*Akis spinosa*, *Scaurus striatus*), the usual host being *Asopia*. Grassi and Rovelli[199] (1889), determined the migration of this worm by feeding the larvæ obtained from *Anisolabis* to a man, as also to white rats. Zschokke[211] (1892) cites the five cases known to have occurred in the human subject, the same being widely distributed (2) in America, (2) in Italy and (1) in France. (See also in this connection Blanchard[202b] (1891), Lutz[216] (1894), Railliet[242] (1895) and Magalhães[221] (1896).

Hymenolepis microstoma (Duj.).

A tape-worm of *Mus rattus* and *M. musculus*, the cysticercus being found in the meal-worm (*Tenebrio molitor*), which has devoured the fæces of infected rats and mice, Grassi and Rovelli[199] (1889) showed that the cysticercoid of Stein found in *Tenebrio molitor* was not the larva of *Hymenolepis murina* (Duj.) as had been previously supposed, but of *H. microstoma*. (*H. murina*, according to Grassi, requires no intermediary host for its development.) The encapsuled larvæ of *H. microstoma* are devoured with the meal-worm, and develop in the intestines of rats and mice into tape-worms. (See Blanchard[202b], 1891, Leuckart[181], 1876; Stein, Zeitschr. f. wiss. Zoöl., IV, 1853, pp. 205 to 212, Taf. X, Moniez, "Essai monographique sur les cysticerques, Paris, 1880, pp. 75 to 79, von Linstow[223], 1897.)

Hymenolepis uncinata (Stein).

Tape-worm of *Crocidura leucodon* and *C. aranea*, the cysticercus being found in a beetle (*Silpha laevigata*), Blanchard[202b] (1891).

Hymenolepis scalaris (Duj.).

Tape-worm of *Crocidura aranea*, the cysticercus occurring in a myriapod (*Glomeris limbatus*) Blanchard[202b] (1891).

Distomum ascidia van Benedan[181], 1873.

According to von Linstow[195] (1887), the occurrence of *Distomum* in bats can only be explained by the fact of their devouring such insects as pass a part of their life in water, the cercaria which have developed in mollusks boring their way into the aquatic larvæ of the insect. The parasites remain in the insect after it has turned into a fly, and the latter infect the bats which devour them.

von Siebold[177] (1844) had observed distomes lying encysted in adult *Ephemera vulgata*. The boring apparatus ("Stachel") could always be observed in the cysts, and, from its resemblance to that of *Cercaria armata*, he concluded these might be embryos of this parasite. To test this, he took *Ephemera* and *Perla* larvæ, and placed them in a vessel containing many *Lymnaeus stagnalis*, which contained *Cercaria armata*. Soon many of the parasites were seen to wander out of the mollusk and attack the insects, boring their way through the soft interarticular membranes. He watched the process with the microscope through the transparent cuticle of the insect. As soon as the boring apparatus had penetrated, the parasite followed, leaving its tail outside, where, after a while, it was torn off. The parasite then became rounded and enclosed in a cyst. He had seen similar parasites in other insects, and believed the latter to play an important role as hosts of other similar parasites. von Linstow states that the parasite is also found in the aquatic larva of *Chironomus plumosus*.

von Linstow[189 195] (1884 and 1887) found *D. ascidia* in two species of bats, *Vesperugo pipistrellis* and *V. Nathusii*; it also occurs in other bats. He considers *D. ascidia* and *C. armata* to be identical.

Distomum endolobum Duj.

This parasite is found in frogs, the aquatic larvæ of various insects serving as intermediary hosts. The development of the parasite was established by von Linstow[195 205 217 228] (1887, 1891, 1894 and 1897). The cercaria bores its way into the aquatic larva of the insect, and becomes encysted in the adipose tissue, forming cysts measuring 0.18 to 0.26 mm. (For a description and figures of the parasite see von Linstow, Archiv f. Naturgeschichte, 1879, p. 185, and his later papers already referred to). von Linstow

found the parasite in the aquatic larvæ of *Limnophilus lunatus*, *L. flavicornis*, *L. rhombicus*, *L. griseus*, *Anabolia nervosa*, *Cloëon dipterum* and *Ephemera vulgata*. Once he found them in the adult insect of the last-named species. He fed *Rana temporaria* with the larvæ of the parasite taken from the insect hosts, and, killing the frog after 13 days, found the adult distomes in its intestine. The parasites now measured 1.02 to 4.5 cm. Frogs may already become infected in the legless tadpole stage.

Distomum isoporum Looss, 1894.

von Linstow[223] (1897) found what he believes are probably the larvæ of this *Distomum* in *Ephemera vulgata*, *Chaetopteryx villosa* and *Anabolia nervosa* caught near Göttingen. The parasites were encapsuled. von L. considers *D. isioporum* identical with *D. longicolle* Frölich and *D. globi porum* Olsson. This species lives in the intestine of *Squalius cephalus*, *Phoxinus laevis*, *Cyprinus carpio*, *Leuciscus rutilus*, *Abramis brama*, *Tinca vulgaris* and *Esox lucius*. The cercaria occurs according to Looss in *Cyclas cornea* and *rivicola*.

Gordius tolosanus Duj., 1842.

This parasite occurs in various beetles, the intermediary hosts being the aquatic larvæ of different insects, whilst the mature worm lives free in the water.

Meissner[178] (1855) was the first to observe the entrance of the first or embryonal larval form of the parasite into a host. He found that they had bored themselves by preference into the larvæ of *Ephemera*, more rarely into those of *Phryganids* and *Diptera*, into *Cyclops* and mollusks. (See Plate II, figs. 1 to 6.) The minute larvæ of the parasite (fig. 3) were seen to lie still in the water, only now and then protruding or retracting their boring apparatus (as in figs. 1 and 2). He was able to determine that they bored their way through the interarticular membrane of the legs of the transparent *Ephemera* larvæ, and could watch them wandering into the trunk of the insect (fig. 4). In the larvæ of the insect, which had been placed in a vessel with many of the parasites, as many as 40 could be counted within the host. When the *Gordius* has reached a suitable resting place, between the muscles, in the sexual organs, the adipose tissue, etc., it draws in its

boring apparatus, bends itself double again so that it looks as it did originally in the egg (figs. 1 and 2), undergoing no alteration during the whole process, except that cysts (figs. 5 and 6) are formed about them. Villot[182] (1874) observed this first or embryonal larval stage of the parasite in *Tanypus*, *Corethra* and *Chironomus*, von Linstow[205] (1891) in the aquatic larvæ of *Sialis lutaria* and ——————[215] (1893) in the larvæ of *Cloëon dipterum*.

The second large larval form of the parasite was observed by Villot[182] (1874) in beetles: *Carabus hortensis* Fabr., *Procerus* (*Carabus*) *coriaceus* L., *Calathus fuscipes* Goeze = *cisteloïdes* Panzer, *Poecilus lepidus* Fabr., *Molops elatus* Fabr., *Pterostichus metallicus* Fabr., *P.* (*Omaseus*) *vulgaris* L., *P.* (*Omaseus*) *melas* Creutzer, *P.* (*Omaseus*) *nigritus* Fabr., *Harpalus atratus* Latr. = *hottentotta* Duftschmidt, *Amara similata* Gyll., *Calathus ambiguus* Payk., *Amara fusca* Sturm, *Zabrus* (*Pelor*) *blaptoïdes* Creutz. and *Silpha carinata* Illig.[1] von Linstow[200] (1889) found them in *Pterostichus niger* Schaller, and states that they had been previously observed in this beetle, as also in *Procrustes coriaceus* Lin., and *Calathus cisteloïdes* Panzer.

It was von Linstow[207] (1891) who determined the evolution of *Gordius tolosanus* in these two sets of hosts. The first or embryonal larvæ of the parasite, being found by him in the aquatic larvæ of *Sialis lutaria* Lin., and *Cloëon dipterum* Lin., where it lies in the adipose tissue and muscles of the insect (fig. 7). The larvæ lie doubled up in a rounded covering of connective tissue. The young parasites bore their way into these insects in summer, and pass the winter within this host, which in May turns into a winged insect. The latter is slow in its movements, and creeps about on the low-lying vegetation near the water, where it falls an easy prey to the beetles. Thus it is that the beetles become infected. During the summer, autumn and winter the parasite grows within the beetle, which in spring in searching for food which is more plentiful near the water, frequently falls in and thus returns the parasite to its proper element. In April, 1889 and 1890, von Linstow observed many land beetles (*P. niger*) on the surface of ditch-water about Göttingen, in the same places where

[1] von Linstow changed the nomenclature in Villot's list which I compared. I have kept to that adopted by von Linstow as being the most recent.

he had found the sexually adult *Gordius tolosanus* swimming about in the summer. Some beetles were dying or dead, and tangled in masses of algæ, whilst others were swimming on the surface and trying to reach the bank. Of 49 beetles taken from the water 10 contained each a single large larva of *Gordius tolosanus* (fig. 9). These larvæ measured 122 mm., and exhibited the boring apparatus at the head. He once saw the large larva bore its way out of the beetle, and found it later lying free in the water alongside the insect. Besides the parasite, only the intestines remain in the beetle's abdomen, the sexual organs and adipose tissue having evidently served for the nourishment of the parasite. When the beetle has fallen into the water the parasite escapes, soon becomes sexually ripe, and fertilization having taken place, the females wind themselves about aquatic plants to which, during the course of the summer, they attach their eggs. The process of egg-laying lasts about four weeks, and about as much time is required for the development of the embryo within the egg. As Meissner has shown, the embryo is 0.065 mm. long and 0.018 mm. wide being armed anteriorly with a boring apparatus with which it penetrates the egg membrane. Having freed itself, the embryo sinks to the bottom, where it moves about slowly in search of a suitable host into which it can bore its way.

von Linstow believes that beetles and flies may infect fish with *Gordius*. Large parasites of the kind having been found in *Thymallus vulgaris*, *Salmo* (spec. ?), *Trutta fario*, *Coregonus Wartmanni*, *Aspius rapax* and *Abramis brama* (E. Dallmer, "Fische und Fischerei im süssen Wasser," Schleswig, 1877, p. 59). As the ponds and pools often dry up in summer the *Gordius* is kept alive by its parasitism in the beetles, and the latter also serve to disseminate the worm.

The occurrence of *Gordius* as a pseudo-parasite of man is mentioned by Railliet[242] (1895), who cites the cases known. See also Blanchard[224] (1897).

Gigantorynchus gigas (Goeze).

This worm (syn. *Echinorynchus gigas*, Goeze, 1782, etc.) is a parasite in the intestine of the pig, wild boar and pecari. Lindemann (cited by Railliet[242]) claims that it is frequently found in man along the banks of the Volga. Schneider, in 1868 ([180] 1871), showed that the larva of the cockchafer or May-bug (*Melolontha*

vulgaris), as also the adult insect, may serve as the intermediary host. Kaiser (1887) showed that the larvæ of the green-rose beetle (*Cetonia aurata*) may also fulfill this function. Stiles[206] (1891) fed the larvæ of a beetle (*Lachnosterna arcuata*) which has similar habits to the preceding species, and proved this insect to be an intermediary host of the parasite in America. Stiles thinks it is probable that a number of species (there are 91 known) of the genus *Lachnosterna* may serve as hosts in America. Schneider found that the larvæ of *Melolontha* became infected by devouring the excreta of pigs which contain the eggs of the worm. The embryos become free after entering the digestive tract of the insect, and, boring their way through the intestinal wall, encyst themselves in its body cavity, where they remain throughout the subsequent stages of the development of the insect. Karsch[190] (1886) says that pigs are very fond of devouring cockchafer larvæ, whilst children and even adults in some places like to eat the raw beetles on account of the nut-like flavor of the thorax. Kaiser[213] (1893) says that the eggs of the worm may lie scattered about with the fæces on the ground, exposed to the weather for weeks and even months, until they are fed on by the insects named. Free-moving embryos appear in the insect's intestine a few days after the ingestion of the eggs, and by means of their hooklets they bore their way through the intestinal wall. (See this publication for details and figures.) The *Melolontha* larvæ with which he experimented all died after a shorter or longer time (usually in a few days) from the effects of the parasites. *Oryctes nasicornis* also served as a host, but Kaiser does not believe that these insects play the rôle that *Cetonia aurata* does, which he regards as the proper host. He states that the worm is only found in large herds of pigs which are driven into the woods to fatten by feeding on acorns. The larvæ of *Cetonia* are found near ant-hills, as also about the roots of oak trees, where the pigs find and devour them. The infected larvæ of the beetle are digested in the intestine of the pig, the worm-embryos are set free, become attached to the intestinal mucous membrane, and gradually attain maturity. Thus the cycle is completed.

Gigantorynchus moniliformis (Bremser).

This parasite (syn. *Echinorynchus moniliformis*, Bremser, 1819) occurs, according to Bremser, in the intestine of the hamster

(*Cricetus vulgaris*) and meadow mouse (*Arvicola arvalis*). Grassi and Calandruccio[192] (1888) also found apparently the identical worm as a parasite of *Mus decumanus* and *Myoxus quercinus* in Sicily. These authors found that a very common beetle (*Blaps mucronata* Lat.) served as the intermediary host. Three times, more than a hundred of the parasites were found in single beetles. The young echinorynchus is visible to the naked eye and lies encysted in the insect and exhibits the chief characteristics of the developed worm. (See plate III, fig. [a, b, c].) Calandruccio infected himself by swallowing these embryos, and a white rat was similarly infected.

Filaria rytipleurites Delonchamps, 1824.

Delongchamps discovered the parasite encysted in the adipose tissue of the oriental cockroach (*Periplaneta orientalis*). If the cysts are removed from the insect and placed in a suitable fluid, the worms bore their way out and may live three or more days in a free condition. These embryo worms are 11-16 mm. long. Galeb[187] (1878) fed 3 white rats with infected cockroaches. He killed the rats after 8 days and found the parasites, which had thrown off their envelopes, in the stomachs of the rats, in the folds of the mucous membrane. In one rat three females and one male were found, all of them being perfectly developed. According to Galeb, fertilization takes place in the rat's intestine and the eggs escaping with the fæces are devoured by the cockroaches. The embryos escape from the egg membranes after they have entered the alimentary canal of the insect, and boring their way through the intestinal wall become encysted in the adipose tissue. The rat infects itself by feeding on cockroaches. Galeb also noticed rat-hairs in the intestines of the cockroaches, these having been given off in the rat fæces in consequence of the animals licking themselves.

Filaria strumosa Rud.

This parasite has been found in moles. von Linstow[189b] (1885) found it in the stomach of *Talpa Europea* L. He claimed subsequently[195] (1887) that he had found the larvæ encysted in the adipose tissue of a beetle (*Cetonia aurata*) which was caught in

the autumn. (He figures both the adult worm and larva in his publications.)

Spiroptera sanguinolenta Rud., 1819.

This nematode is a parasite of the dog, wolf, and perhaps of the fox and other carnivora. It is usually situated in tumors of the esophagus or stomach, but it has also been observed free in the esophagus, in an aortal tumor, in lymphatic ganglia, in the lung, etc. In China the parasite is found in 10 per cent of the dogs. Grassi[197] (1888) found that the oriental cockroach (*Periplaneta orientalis* L.) is the intermediary host. He fed dogs in Catania with infected cockroaches and killed them after 5-15 days. He then found adult worms burrowed in the esophagus and stomach of the dogs. Control dogs showed none of the parasites. Grassi believes that other insects may also serve as intermediary hosts, but it appears as if the usual host were the cockroach. These insects are very plentiful in Catania and a veritable scourge in Southern Italy, where dogs are very generally affected by the parasite. Grassi states that dogs like to hunt after cockroaches. (See further, Railliet[242], 1895, pp. 537-538.)

Spiroptera obtusa.

Leuckart found this parasite encysted in *Tenebrio molitor*, the fully-developed worm being an intestinal parasite of the mouse.

In the case of the *Filaria immitis*, Leidy, 1856, and *Filaria attenuata*, the intermediary host is unknown:

Filaria immitis.

The adult worm is found chiefly in the right heart of the dog. Thousands of embryos given off by the female circulate in the blood. The embryos exhibit to a certain extent the periodicity observed by Manson in *Filaria sanguinis hominis*, the parasites being most numerous at night. Bancroft had claimed to have found the embryos in *Trichodectes* to which he attributed the role of intermediary hosts. Sonsino[198] (1888) held the same opinion. Both of these investigators were wrong, as *Trichodectes canis* does not suck blood. Sonsino next attributed this role to *Hæmatopinus pilifer*. Both Grassi and Sonsino observed nematodes in the intestine and body-cavity of dog-fleas, which they thought were embryos derived either from *Filaria immitis* or *Spiroptera sanguinolenta*. It was subsequently determined that the latter parasite does not give off hæmatozoal larvæ, whilst Grassi[197] (1888) conclusively proved (as against Sonsino) that neither *Pulex serraticeps*, *Hæmatopinus* nor ticks (*Rhipicephalus*

siculus, Koch) served as hosts for the embryos of *F. immitis*. Sonsino was led astray by the coincidence that *Filaria recondita* Grassi (see below) was present in the dogs he examined and he took the embryos of the latter, as Grassi showed, for those of *F. immitis*. Consequently the evolution of *F. immitis* remains to be determined. Grassi thinks the intermediary host may be a crustacean or mollusk.

Filaria attenuata.

The embryo of this parasite does not develop in the crow-louse according to Grassi[197] (1888, p. 776), neither do these lice suck blood. The probably identical *Filaria* of *Garrulus glandarius* does not find intermediary hosts in other species of blood-sucking lice found on this bird.

Filaria Bancrofti Cobbold, 1877.[1]

The idea that the mosquito might serve as a carrier of the *Filaria sanguinis hominis nocturna* seems to have occurred almost simultaneously to Bancroft in Australia, and Manson in China. In a letter dated 20th April, 1877, from Brisbane, Bancroft wrote to Cobbold[247] (1878): "I have wondered if mosquitoes could suck up the hæmatozoa and convey them to water. I will examine some mosquitoes that have bitten a patient to see if they suck up the filariæ." In a letter dated 27th November, 1877, from Amoy, Manson wrote to Cobbold[247 248] about his observations on the development of the parasite in the mosquito, etc., and sent on his manuscript for publication. According to Manson[250] (1878) the embryonic form of the *Filaria sanguinis hominis*, when ingested by the female mosquito with the blood of the infected human subject, undergoes certain developmental changes. A few days after gorging itself with blood, the mosquito seeks the water, lays its eggs, and dies, setting the filariæ free, and thus rendering the water a vehicle for the infection of man.

Manson procured and infected mosquitoes by placing a patient whose blood contained filariæ in a room where mosquitoes were

[1] The *Filaria sanguinis hominis*, the embryo of *F. Bancrofti* was discovered by Lewis in 1872, and two years later Sonsino observed it in Egypt. In 1876 Bancroft in Australia discovered and described the parent worm which he found in patients suffering from hydrocele or lymphscrotum, etc., in conjunction with filariæ. Cobbold[247] (1877), who announced Bancroft's discovery, named the parasite after him. Other blood filariæ having since been discovered, Manson[252] (1891) has suggested that a fourth name be added to distinguish them. He names three species in this way: *Filaria sanguinis hominis nocturna*, *F. s. h. diurna*, and *F. s. h. perstans*. The first form is that which concerns us. The development of the other two is unknown.

plentiful. After the patient had gone to bed, a light was placed beside him and the door left open for the mosquitoes to enter. When a sufficient number had accumulated, the light was put out, and the door closed. Next morning a large number of mosquitoes filled with blood were readily caught by means of an inverted wine glass. They were then temporarily paralyzed by a whiff of tobacco smoke, and transferred to small vials which contained a little water. The blood in the stomach of the mosquito seemed to contain more filariæ than an equal quantity of blood taken directly from the patient. In a later publication Manson[258] (1883) said that he considered the filarial lash assisted in the transference of the parasite to the mosquito. He observed that the embryo in lymph from the scrotum of a filarial subject, collected in large numbers about a few cotton fibers that had been dropped into the fluid, the parasites beset the fibers in every possible fashion, in groups, in lines and singly, most of them being attached by their head or tail lashes which were wound firmly around the fibers. He thinks the filariæ become similarly attached to the proboscis of the mosquito, whilst the insect is sucking blood, and that this accounts for the greater number found in the insect's stomach, as compared to the number observed in an equal quantity of blood taken directly from the filarial patient. In his first publication Manson (1878) writes that by far the greater number of filariæ ingested by mosquitoes die and are disintegrated, or expelled in the insects' fæces. Only a few are seen to undergo metamorphosis. The embryo is at first perfectly structureless, being enclosed, as Lewis had originally observed, in a delicate, usually closely applied tube, within which it extends or shortens itself, "giving rise, from the collapse of the tube when the body is retracted at either end, to the appearance of a lash at the head and tail." (See figures *a-g*, Plate II, taken from Lewis (1879) and *h* from Manson[259], April, 1884.) A few hours after the ingestion of the filariæ by the mosquito, changes begin to be noticeable. The tube separates from the body, giving rise to a double contour, and the body exhibits transverse striation. The sheath is either digested by the gastric juices, or ruptured by the filaria, which becomes free and more markedly striated. The striation then disappears, and the parasite becomes granular, the movements being less active. After 36 hours it ceases to move actively, grows shorter and broader,

the granulation becoming finer. By the end of the third day, the tail appears to spring abruptly from the end of the sausage-shaped body, and large cells may be distinguished in the hitherto homogeneous protoplasm, whilst it presents sometimes a double contour. Indications of a mouth, and (through pressure) of an anus, a little in advance of the tail, are seen. The parasite now becomes elongated, the mouth acquires 3 or 4 lips, and the alimentary canal is indicated by a delicate but distinct line running from mouth to anus. Movement is now feeble, being confined to the caudal appendix, which gradually disappears. As most mosquitoes died on the fourth to fifth day after feeding, later developmental stages were but rarely observed. The most highly-developed parasites (fig. *h*), four of which came under examination, were visible to the naked eye; they measured $\frac{1}{16}$ of an inch in length by $\frac{1}{825}$ of an inch in breadth, the original embryos measuring $\frac{1}{100}$ of an inch in length. The large cells which had made their appearance within the parasite, have now become smaller and are gathered around the dark line which represents the alimentary canal. "In this way an alimentary tube is fashioned, and the peculiar and characteristic valve-like termination of the esophagus in the intestine, seen in *Filariae* is developed. The mouth may now be seen open and funnel-shaped, and the tail is reduced to a mere stump." The movements now become brisker, the body elongates, all cellular appearance vanishes, and owing to the increased transparency of the tissues, the details, except a line indicating the intestine, can no longer be made out. The one tapered extremity is crowned by papillæ; Manson being unable to determine if there were 3 or 4 of these. He thinks this may constitute the boring apparatus with which the parasite makes its escape from the mosquito, and penetrates the tissues of man. In this, presumably the last stage of development within the mosquito, the parasite "becomes endowed with marvelous power and activity. It rushes about the field, forcing obstacles aside, moving indifferently at either end, and appears quite at home, and in no way inconvenienced by the water in which it has just been immersed. This formidable-looking animal is undoubtedly the *Filaria sanguinis hominis* equipped for independent life and ready to quit its nurse,[1] the mosquito." According to Manson, the para-

[1] Intermediary host is meant.

site next escapes from the insect into the water in which the latter has died, man becoming infected by drinking the water containing the *Filariae.* The *Filariae* bore their way through the human intestine, find a suitable resting place there, become perfectly developed, and, fecundation having been effected, new swarms of embryo-filariæ are given off into the warm-blooded host, in this way completing the cycle of development.

Lewis[249] (1878) made similar observations in India. Of 140 female mosquitoes examined by him 20 contained filariæ. After the third or fourth day no active filariæ could be found in the mosquito's digestive tract, and on the fourth or fifth day they had all been apparently digested and excreted. He writes: "It was observed that nearly all the mosquitoes captured in one of the servants' houses contained hæmatozoa, so that the supply of suitable insects in all stages of their growth became amply sufficient for all requirements. The result of the examinations under these favorable conditions has shown that although the stomach digests a great number of the ingested hæmatozoa, as mentioned above, nevertheless others actually perforate the walls of the insect's stomach, pass out, and then *undergo developmental changes in its thoracic and abdominal tissues.*" . . . "It should be added that the blood of one of the five persons who were in the habit of sleeping in the house in which these particular insects were captured,, was found to contain the hæmatozoa in considerable numbers." Lewis does not think these "observations are sufficiently conclusive to warrant a positive statement being made at present, for, though assuming that, of the various parasitic forms which have been seen, several are actually transitional stages in the development of one and the same entozoön, it is to be noted that even the most advanced stage hitherto observed is still a very immature one, no trace of reproductive organs, for example being distinguishable; and every attempt hitherto made by myself, to obtain a more advanced condition has proved unsuccessful." In a publication which appeared a year later Lewis[251] (1879) describes and figures the changes undergone by the filaria in mosquitoes (see Plate II). Araujo at Bahia verified the occurrence of filariæ in mosquitoes in 1878, and believed the mosquito to be the intermediary host (Cobbold[248] 1878). Bancroft[252] (1879) writes that he counted 45 filariæ in a single mosquito that had sucked the

blood of a filarial patient. (See also a pamphlet published by Bancroft in Brisbane entitled "Plants and Animals, etc.") Myers[256] (1881) observed that filariasis did not spread in Formosa, whilst the disease abounds on the mainland 180 miles off. He makes the suggestion that perhaps the proper mosquito does not occur on the island. Only 3 cases occurred in Formosa in 9 years, amongst 15,000 hospital patients, and all three came from the mainland. There are plenty of mosquitoes in Formosa. He placed a filarial patient under a net with mosquitoes. All the filariæ which the mosquitoes ingested were digested, as Manson had found with dog-filariæ. Sonsino in Cairo wrote to Manson[258] (1883) stating that he had observed the metamorphosis of the parasite in the mosquito. He[260] (1884) once (working with *Culex pipiens*) saw the development reach the sixth stage described by Manson. Sonsino found that fleas and bugs were not suitable hosts (Railliet[242], 1895, p. 519).

A slight difference will be noted between the descriptions of the metamorphosis given by Manson and Lewis. Lewis saw no marked changes within the first 24 hours, whilst Manson says that after 3-6 hours the movements of the filaria become languid and marked separation of the sheath occurs, after 8 hours the sheath disappears, etc.[1] Whilst Manson appears to have only followed the development of the parasite in the intestine, Lewis observed it in the parasites which penetrated into the insect's tissues. Manson observed a more highly developed form than Lewis.

Periodicity.

Manson (1881), and afterwards Mackenzie[254 255] and Myers[256] in the same year, found that the *Filaria* embryos appeared and disappeared periodically from the blood. Manson "watched it preserve its rhythm for a month on end," that is, the filariæ appeared towards evening, increased in numbers during the night, and decreased in the morning. Mackenzie, who studied a case in London, found that if the filarial patient was kept up all night and allowed to sleep during the day the periodicity above referred to

[1] Neither of these authors states the temperature at which the mosquitoes were kept; this probably has a considerable influence on the rate of the parasites' evolution.

was reversed, that is, the parasites appeared in the blood during the day and disappeared at night. Myers found that the filariæ appeared regularly between 6 P. M. and 8 A. M., being most numerous at midnight. At first the parasite is very active, then it grows torpid and feeble, being shriveled and straightened out when disappearing. He thinks a new lot of embryos are produced regularly by the parent worm, and that they die off in the blood. Manson[258] (1883) considers that "*filarial periodicity is an adaptation of the habits of the filaria to those of the mosquito*, the intermediary host indispensable to the future life of the parasite." He was able to confirm Mackenzie's observation on the periodicity becoming reversed when the patient is kept up all night. According to Manson it is not simply sleeping or waking that causes this periodicity, but something that recurs every 24 hours. That sleep does not cause it is evident from the circumstance that the ingress normally occurs hours before the usual time for waking. Manson gives a detailed description of his observations on periodicity and the variations in the number of filariæ in the blood.

Interesting are similar observations of Grassi, to which we shall now refer, wherein it is shown that the embryos of *Filaria recondita* undergo developmental changes in fleas and a tick.

Filaria recondita Grassi, 1890.

(The embryo being the Hæmatozoön of Lewis.)

Grassi[201] (1890) succeeded after much difficulty in finding a not quite adult female of this worm lying, not encysted, in the adipose tissue near the hilum of a dog's kidney. In 1888 Grassi[197] had observed that a great resemblance existed between the embryos of this worm, as found in fleas, and those described by Manson as occurring in the mosquito (*Culex pipiens*), which the latter regarded as stages in the development of *Filaria Bancrofti*. Grassi saw 30 to 50 embryos in a single flea, and found them in various stages of development, both in the intestine and body cavity of the insect. The parasites also exhibited the sausage shape and the form with three caudal papillæ, such as Manson described in the *Filaria sanguinis hominis* within the mosquito. As Grassi (1890) was able to determine, the Hæmatozoön of Lewis

undergoes a metamorphosis in the dog-flea (*Pulex serraticeps*) in the cat-flea (which is regarded by many as but a variety of the preceding), in *Pulex irritans*, which is often found on dogs, as also in a tick (*Ripicephalus siculus* Koch). The embryos of this filaria, which were first described accurately by Lewis[183] (1875) were found by Grassi to perforate the intestinal wall of the flea, which had ingested blood containing the parasites. The latter then make their way into the fatty tissue, where they are almost always to be found lying singly in the fat-cells. The fat-cells increase in size as the parasites grow, the latter being curled up once or twice within the cell, the nucleus of which remains uninjured. Grassi believes that the parasites may also develop outside of cells, and he has sometimes seen them in fleas' *eggs*,[1] as also in the cysticercoid of *Dypilidium caninum*. The embryo of the filaria undergoes four stages of development in the flea, in which insect Grassi and Calandruccio[201] studied the evolution especially. (See figures 1-13, Plate I, and the explanation accompanying the plate). The worm was observed to nearly attain its complete development in the flea. (Stages III and IV.) Infection experiments with fleas did not give a positive result, which may be due to the fact that the parasites were not fully developed. Grassi dwells on the resemblance between his observations and those of Manson on *Filaria sanguinis hominis*.

Tsetse-Fly Disease.

The ravages caused by the tsetse-fly are well known in the history of African exploration. Livingstone[235] (1857), Green and other travelers in Africa have lost large numbers of animals from the disease which they convey. Livingstone attributed the fatal effects of the tsetse-fly to the influence of a venom which they injected into the animals they attacked. The greater number of authorities, Mégnin[236] (1875), Veth, van der Wulp[239] and van Hasselt (cited by Marshall[237], 1883), Schoch[238] (1884), Railliet[242] (1886), Laboulbène[240] (1888), Blanchard[241] (1890) and others, held, however, to the opinion that the tsetse-fly only served as a carrier

[1] This is interesting when we consider Texas fever. The parasite of this disease has not been found as yet in the eggs of the tick, but might be found if further search is made. See under Texas fever.

of an infectious agent, similar, perhaps, to that of anthrax. The disease seems to prevail more or less throughout Central Africa. Scloss states it is called "la mouche" on the Congo, Livingstone and Oswald (1849) refer to it on the Zambesi, Bruce has studied it in Zululand, and Koch has found the disease prevalent in the East African German Protectorate. The disease is confined to low-lying, moist regions along rivers and near the seacoast, these regions being well known as especially dangerous to cattle and horses. In Zululand they speak of such a region as the "fly country." Under the name of tsetse-fly are comprised, according to Railliet[242] (1895), several species of *Glossina*; but one species, the *Glossina morsitans*, Westwood, 1850, seems to have been chiefly studied.[1] Descriptions and illustrations of this fly are given by Blanchard[241] (1890), Railliet[242] (1895) and others, whilst an excellent colored plate, as well as photographs, will be found accompanying Bruce's[244] (1896-97) second report on "Nagana," by which name the disease is known in Zululand.

The domesticated animals which suffer from the disease are the horse, mule, donkey, cattle, dog and cat. Of 35 wild animals investigated by Bruce, 10 contained the parasite which he had discovered in their blood. These comprised 1 buffalo, 3 wildebeests, 3 koodoos, 1 bush-buck and 1 hyena. In 1895 Bruce[243] discovered that the tsetse disease, or Nagana, is due to a hæmatozoal flagellated micro-organism, bearing a close resemblance to *Trypanosoma Evansi*, which is the cause of a similar and perhaps identical disease in India known as surra.[2] Bruce found that the disease could be conveyed from sick to healthy animals through inoculation with small quantities of blood containing the parasites, and was able to demonstrate in the most conclusive manner, by experiment, that the *Glossina morsitans* does convey the infection from diseased to healthy animals.

Under natural conditions the tsetse-fly apparently becomes con-

[1] Bigot, J. M. F. (Genre Glosina. Annales Soc. Entomol., France, 1884, vol. v, p. 121-124), gives a list and synopsis of 6 species known: *G. longipalpis* Wd. (*Nemorhina palpalis* R. D.), *G. fuscus* Wlk., *G. tabaniformis* Westw., *G. morsitans* Westw., *G. tachnoïdes* Westw., and one new one.

[2] Koch (1898) considers that Surra may also be conveyed by biting insects in India; other views have prevailed there hitherto, infection being attributed by Lingard and others to infected food and drink. Koch assumes, I think, quite prematurely that Surra and Nagana are identical.

taminated by biting wild animals.[1] In support of this may be cited the fact, repeatedly observed, that Nagana disappears among domesticated animals when the wild ones have left the district. The natives considered that the wild animals infect the soil and water and that these give rise to the disease amongst their cattle or horses. Bruce twice found the *Glossina* sucking blood from the carcasses of wild animals, once on a buffalo and once on a wildebeest. That the *Glossina* is not capable *per se* of producing Nagana was proved by catching them and keeping them hungry a few days before they were allowed to bite susceptible animals. *To convey the disease the contaminated flies must bite a healthy, susceptible animal soon after they have been on a diseased animal, or been caught in the fly country.* Bruce took horses into the fly country from Ubombo, which occupies an elevated position where Nagana does not occur, and exposed them there for some hours to the bites of the *Glossina*, at the same time excluding the possibility of their becoming infected by water or vegetation. The horses invariably acquired Nagana. He then caught flies in the fly country and brought them in gauze bags to Ubombo (this took 4 to 7 hours) and placed them on healthy horses; the result was the same. Up to 46 hours after the flies had sucked infected blood, the trypanosomes were to be found alive in the insects' proboscides. Motile parasites were still found in the flies' stomachs after 118 hours, but after 140 hours their stomachs were empty, and apparently dead parasites were found in the excreta. If contaminated flies were kept 12 to 48 hours before they were allowed to bite healthy dogs, these only sickened on the 32d to 38th day instead of after two weeks, as is usually the case. In two out of three inoculations made with Nagana blood which had been dried on threads for 24 hours, the result was negative. Nagana blood removed and preserved aseptically still caused the disease if inoculated after 4 days, but it did not do so after 7 days. We can now understand why Nocard and Railliet (Railliet[242], 1895) obtained a negative result from an inoculation made on a sheep with the head and proboscis of a tsetse-fly from Zanzibar. Other flies do

[1] The disease probably runs a long-continued course in some wild animals as it does sometimes in cattle, some of which have been observed to recover. Bruce once found the parasites in the blood of a cow 18 months after inoculation.

not seem to convey the disease as do the *Glossinae*, for there were plenty of the former at Ubombo, but the disease was never conveyed there to healthy animals though these were kept together with diseased ones. The *Glossina* seems to act, then, as a simple carrier; there is no reason for supposing that the fly acts as an intermediary host for the parasite. In one experiment Bruce cites, a horse at Ubombo was bitten by 129 flies as follows: 22 Nov., 10 flies; 28 Nov., 10; 30 Nov., 9; 1 Dec., 5; 2 Dec., 13; 4 Dec., 20; 6 Dec., 7; 8 Dec., 30; 11 Dec., 11; 14 Dec., 14; the animal showed symptoms of the disease on the 15th of December.[1]

Texas Fever.

The idea that the tick was the cause of Texas fever among cattle had already prevailed among cattle-owners in the United States before Smith began the remarkable researches about to be described, which led to the experimental demonstration of the accuracy of the popular belief. The cattle-tick (*Boöphilus bovis*) was first described in 1868 by Riley under the name *Ixodes bovis*, and in 1889, in view of the suspicion that it played a rôle in Texas fever, Curtice[225] (1891) studied its biology.[2]

The blood-filled tick having dropped off lays her eggs a few days later. The process of egg-laying may last a week or more. After 20 to 45 days the larvæ escape from the egg and attach themselves to the cattle. In two weeks the young tick is sexually ripe, becomes fertilized, and in 21 to 23 days, having filled itself with blood, it drops to the ground and in turn lays eggs. We see from this that a tick-generation has an age of 41 to 68 days. Ten days after the young ticks attach themselves to the cattle, the latter begin to sicken. Smith and Kilborne[226] (1893) found that young ticks could be kept alive for months without food. The cattle-tick may injure its host to some extent by blood-abstraction, but this is usually not serious. The tick "produces more or less inflammation of the true skin and subcutis; where it is attached, sections of the skin examined under the microscope show a very

[1] See in this connection the inoculation experiments of Kanthack, Durham and Blandford, Hygienische Rundschau, 1898, December. Further details will also be found in an article by Nuttall[310] (1898).

[2] See also Bulletin No. 5 n. s., 1896, p. 217, Div. of Entomol., U. S. Dept. of Agric.

intense cell infiltration at the place of attachment, and for several millimeters around it. This infiltration is not noticed by the unaided eye." This local reaction is probably due to the tick's irritant secretions, which prevent the blood from coagulating. "After they have attached themselves, ticks are in communication with blood-vessels, for on removing them a drop of blood oozes from the place of attachment." When the disease appears the ticks are still quite small and may be overlooked; they attach themselves by preference to the tender regions of the hide.

To find out if the disease could be communicated from southern to northern cattle in the same enclosure, without the intervention of ticks, Smith and Kilborne (1889 to 1892) carefully removed ticks from the southern infected cattle. In this way no ticks could mature and infect the ground. The northern cattle all remained healthy, proving that the ticks were necessary to cause the disease. To determine if Texas fever could be produced without the presence of southern cattle and only by ticks, fields were infected (1889 to 1890) with mature ticks and susceptible cattle placed there acquired Texas fever. This proved that the ticks alone could produce infection. Finally Smith and Kilborne demonstrated that young ticks hatched artificially and kept in glass dishes in the laboratory (they were the young of infected ticks dropped from southern cattle) were capable of communicating the disease at any time of the year when placed on susceptible animals.

The period of incubation varies with the time necessary to produce a new generation of ticks. Experiments showed that susceptible northern cattle placed in a field with infected southern cattle usually developed symptoms of Texas fever after 45 days. Deducting 10 days for the development of the fever, we have 35 days left, representing the age of the new tick generation. Cattle placed later on infected pastures are attacked immediately by the young generation of ticks and may die in less than 15 days. Low temperature may considerably prolong the incubation period, because it also retards the development of the young ticks. It has been observed that southern cattle driven slowly northward (taking 25 to 30 days) gradually shed all their ticks, and in the end are no longer infectious to northern cattle.

At first it was thought that the gorged ticks falling off, laying their eggs, dying and disintegrating, infected the fields, so that

cattle feeding on the latter contracted the disease. This was, however, disproved by the negative result of feeding-experiments with adult ticks, tick-eggs and grass from infected fields. That the excreta of infected cattle do not communicate the disease was proved in the experiments where infected cattle free from ticks were allowed to pasture in the same field with susceptible animals. A field on which blood and crushed organs of infected cattle had been spread also did not cause infection. Only two cows became infected in a manner that could not be explained, possibly, Smith and Kilborne think, by biting flies, but this is only a supposition; no ticks could be found on the animals, but as they may be very minute, they may have been overlooked.

Owing to the very minute size of the Texas fever parasite, it has until now been impossible to follow its development in the tick; a number of observers have tried to do so and have failed. Though Smith and Kilborne proved conclusively that the young tick conveys the disease, exactly how it occurs still remains to be investigated. As they say, a complex symbiosis between the parasite, the tick and cattle seems to exist, and it appears possible that the parasite may become localized in certain glands of the young tick. The parasite has been found in small numbers in the blood of apparently healthy southern cattle, so that these, if ticky, are also capable of spreading the disease. These cattle seem to tolerate a certain number of parasites without injury, and it is possible that they are constantly reinfected by the ticks. The infectious agent of Texas fever is transmitted with undiminished virulence from one tick generation to another. It is almost superfluous to refer to the inaccurate observations of Billings[229] (1893), who at one time claimed that he had discovered a bacterium which was the cause of Texas fever. Suffice it to say that they served to raise a totally unjust scepticism, especially in Europe, as to the value of Smith's researches. Persons who had never seen Texas fever or perhaps even read Smith's original publications, did not hesitate to give adverse opinions. I do not think it necessary to quote these, for the accuracy of Smith's observations has been since proved by others.

The next step was to put to practical use the knowledge gained, and experiments have since been conducted on a large scale to find a means of ridding southern cattle of their ticks. Nörgaard[232]

in 1895 and 1896 published a report stating that the ticks could be removed effectually by bathing cattle in vats containing certain solutions. It was difficult to find a bath which injured the tick and not the cattle. 25 per cent glycerine was effective but naturally too expensive. The best results were obtained with chloronaphtholeum, 2 per cent (50 pounds), with 40 pounds of soap in a vat 5 feet deep containing 2500 gallons of water. 24 hours after dipping all the smaller ticks were dead, also many gorged ones. After 4 to 5 days all the ticks had turned black and died.

Ticks have also been found associated with Texas fever by Pound[230] and by Hunt[230] (1895) in Australia. Pound recommends burning off the grass on infected pastures as a prophylactic measure. Hunt claimed to have found the parasite in young ticks, but this seems scarcely credible, as various trustworthy investigators in the United States have been unable to find them. Hunt, as well as others, failed to produce Texas fever by injecting crushed young ticks hypodermically, it being impossible at present to offer an explanation of the fact. Hill[231] (1895) found ticks on cattle suffering from Texas fever in California. Since Smith's publication the parasite has also been found affecting cattle in Roumania, South Africa, the Campagna of Rome and in the low country along the Danube. Quite recently Koch[233, 234] (1898, I and II, see under Malaria literature) reported that he observed the disease amongst cattle in German East Africa. The disease extends there along the whole coast, probably throughout the whole of the Portuguese territory and far to the south. He made successful infection experiments with young ticks, for he found ticks on the infected animals. Referring to Smith's observations he says: "I must add that this last experiment with the young ticks has not really found faith with specialists; it does seem too romantic, and also it had not been carried out in a manner sufficiently free from criticism." I believe it was Prof. W. H. Welch who once referred to Smith's experimental demonstration of the rôle of ticks in Texas fever as a "romance in pathology," for such it is most certainly. Those who are familiar with Smith's work will, I think, fail to see the justice of Koch's remark regarding the experiments with young ticks. Smith's experiments deserve no criticism of this kind. Koch repeated Smith's experiments under very slightly altered conditions and confirmed them.

Koch took gorged ticks from (*a*) apparently healthy and (*b*) diseased animals and placed them in separate glass vessels. The ticks laid eggs from which young ones issued, which he transported to Kwai in West Usambara, a ten days' journey from Daressalam, where the parent ticks had been gathered. "Consequently, all objections attributable to accidental infections which might have occurred at the place of origin are excluded." (I think this can also be said of Smith's experiments!) There never had been Texas fever at Kwai. The young ticks were now placed on cattle, and these developed Texas fever on the 22d day. Only those animals acquired Texas fever on which ticks from lot *b* had been placed. It is interesting to note that the animals infected with these ticks, as also such as were inoculated with the blood of such cattle, all went through a mild attack of the disease with the exception of one animal, previously sickly, which died. Koch would explain this by the fact that the young ticks had suffered from the great heat during this journey and the supposition that the parasites they contained suffered correspondingly, thereby losing their virulence. On arriving in Kwai the majority of the young ticks had already died.

Malaria.

(*The mosquito-malaria theory.*)

The theory that the mosquito[1] plays a rôle in malarial infection seems to have existed a long time. It is a fact that the common people in various countries believe in the mosquital origin of malaria. When recently in Italy, Professor Lustig of Florence told me that it has long been a belief among the Italian peasants, and Geheimrath Rubner has also informed me that the same idea prevails in southern Tyrol. Koch[298] (1898, I), in a report on his observations in German East Africa, states that the negro of the Usambara mountains, who acquires malaria when he descends to the lowlands, has also convictions on the subject. "He calls the disease Mbu, and if one asks him where he has acquired it, he replies that there are insects down there which are also called Mbu (*i. e.*, mosquitoes) like the disease—these had stung him, and that is how he had acquired the disease." Dr. Ronald Ross wrote to

[1] **By the term mosquito is meant a variety of different insects—see Appendix.**

me, in a letter dated October 31st, 1898, that a Mr. Jameson in Assam, who has also been in Africa, has informed him that in parts of Africa and Assam the natives believe that mosquito-bites cause fever. The mosquito-malaria theory has certainly existed a long time in the United States.[1] It has long been known, and this in different parts of the world, that curtains, gauze veils, mosquito-nets and the like, protect against malarial infection.

In 1848[2] Nott[80], of New Orleans, published an essay on yellow fever in which he also refers to malaria *as if the mosquito theory had already been advanced*, and he gives grounds for his belief that the mosquito also gives rise to yellow fever. In 1883 a most elaborately stated argument was published by King[278], in which he brings together a mass of evidence on the subject, vastly more, in fact, than other authors have since gathered, and I shall often have occasion to refer to his paper. It is curious to look over the more recent literature on the subject to see how writers have rediscovered the mosquito-malarial theory. In France the theory is ascribed to Laveran, in Germany to Koch and Pfeiffer, in England to Manson, whilst in Italy the names of Bignami, Mendini and lastly, Grassi, are identified with it. By far the most masterly exposition of the theory was written by King. It is first mentioned by Lavaran in 1891, by Manson in 1894, whilst Pfeiffer makes the first published statement of Koch's views in 1892. As far as I

[1] In King's publication[278] (1883) there occurs a reference to a paper by John Crawford, "Mosquital Origin of Malarial Disease," which had remained inaccessible to King, and was said to have appeared in the Baltimore Observer in 1807. Nicolas[279a] (1889) also gives this reference which he must have taken from King. Bignami[289] (1896) seems to have taken it from Nicolas; the latter gives the wrong date, *i. e.* 1867 instead of 1807. It seemed to me a matter of considerable interest to follow up this reference, so I wrote to Prof. King about it. He has been to a great deal of trouble and has found out that the Baltimore Observer, which only appeared in 1806-1807, contains no such article. That Dr. John Crawford considered that insects played a role in the spread of disease, has been noted under the heading "Miscellaneous." Both Prof. W. S. Thayer and Prof. A. F. A. King looked through a review of Crawford's papers which appeared in the Baltimore Med. and Phys. Recorder, 1809, but they found no mention therein of mosquitoes in connection with malaria. I am exceedingly indebted to both the gentlemen above named for the readiness with which they assisted me.

[2] I take this opportunity of thanking Dr. Isadore Dyer of New Orleans, La., for the trouble he took to write out and send me an abstract of Nott's publication, the original being inaccessible to me.

can gather, Bignami and Mendini refer to it in 1896 and Grassi in 1898. It is difficult to say to whom is really due the most credit. I shall not attempt to do so, but will leave it to the reader to draw his own conclusions from the facts here presented.

Laveran[281], in 1891, expressed his belief that malaria was conveyed by mosquitoes, and gave some of the usual arguments in support of the theory. In the same year Flügge[112] wrote "Manche Beobachtungen, so z. B. die Erfahrung, dass die Abend- und Nachtluft vorzugsweise Gefahr bringt, während über Tag die Luft desselben Ortes gar nicht oder selten Infektionen veranlasst, ferner dass oft nach flüchtigsten Aufenthalt auf Malariaterrain sehr rasch Infektion eintritt, legen die Vermuthung nahe, dass der Transport der Erreger zum Theil durch Insekten, namentlich Mücken, Mosquitos, etc., besorgt wird. Diese sind einer solchen Rolle offenbar sehr geeignet, schwärmen vorzugsweise Abends und Nachts und sind eventuell im stande, die Erreger direkt ins Blut einzuimpfen, und so eine Erklärung für die Fälle zu liefern, in welchen schon wenige Stunden nach der Ankunft auf dem Malariaterrain Erkrankung eintritt." Bignami[280], as also Mendini[286], writing in 1896, express similar views.

Prof. Robert Koch has had the kindness to inform me that the possibility of mosquitoes playing a rôle in malaria first occurred to him whilst he was in India in 1883 to 1884, when he had an opportunity of studying the conditions under which tropical malaria occurs. Since then he has always referred to it in his lectures. The first reference in the literature to his views is by Pfeiffer[282] (1892), who writes "Es wäre möglich, dass auch bei den Malariaparasiten exogene Zustände existiren, Entwickelungscyklen, die ausserhalb des menschlichen Körpers, vielleicht im Leibe niederer Thiere (gewisser Insekten z. B.) vielleicht auch zum Theil mindestens im Boden sich abspielten. Diese exogenen Malariakeimen können dann durch die Luft, durch das Wasser oder, worauf *Robert Koch* mich aufmerksam machte, durch den Stich bluts augen der Insekten auf den Menschen übertragen werden." This is the first mention of this subject by Pfeiffer, and Manson[283] first speaks of the probable relation of mosquitoes to malaria in a publication which appeared in 1894. He drew an analogy (as King had done) between the rôle of the mosquito in relation to *Filaria sanguinis hominis* and its possible rôle in malaria, where he considered that

the flagellated form of the malaria parasite represented the first phase in the extracorporeal existence of the latter. These views of Manson's will be again considered below.

King (1883) very[1] properly introduced the arguments which he had gathered in favor of the Mosquito-Malaria Theory with the words, "While the data to be presented cannot be held to prove the theory, they may go so far as to initiate and encourage experiments and observations by which the truth or fallacy of the views held may be demonstrated." I can do no better than quote his words. In the following pages I have incorporated most of King's arguments, and added many data gathered from other writers, as well as some suggestions of my own.

Evidence in Favor of the Mosquito-Malaria Theory.

1. *Malarial Season.*—The malarial season corresponds usually to a period of *warmth* and *moisture*, conditions which are most favorable for the development of the mosquito. Malaria is rarely developed at a temperature below 15 to 16° C., a temperature which is necessary for the evolution of the mosquito, and it is checked at 0° C., at which temperature the mosquito is inactive. (Hirsch,[2] King, etc.) In many places malaria develops after the first rains; the latter may have formed pools in which mosquitoes multiply. Malaria disappears when the rains subside (Bignami) and so do mosquitoes. Malaria often ceases after excessive rains (Hirsch), for then the pools are often washed out and flooded; besides that, excessive rains are always injurious to insect life.[3] Cooke (Tran-

[1] King thinks mosquitoes may even be protective against malaria by their inoculating an attenuated virus. Koch (1898) expresses the same idea. It is worthy of note in this connection that Koch observed a mild form of Texas-fever in cattle on which had been placed young ticks which had been exposed to unfavorable conditions.

[2] Hirsch. Handb. d. hist.-geogr. Pathologie, vol. I, Stuttgart, 1881.

[3] It seems almost superfluous to cite authority for this statement, the observation having been so frequently made. von Nordenskiöld ("Grönland. Schilderung der zweiten Dickson'schen Expedition ausgeführt im Yahre 1883." Leipzig. 1886, p. 75 and 236), who tells of the sufferings due to enormous quantities of *Culex* on the coast of Greenland, observed that continued rains greatly reduced their numbers. They were also not troublesome whilst a fresh sea-breeze was blowing. Weeks[382] (1890) states that heavy showers frequently destroy great numbers of dragonflies. I might add that rain and wind do not only affect the winged mosquito, they will also prevent many from escaping from the puparium, and the process of egg-laying.

sylvanian Journal of Med., 1828, I, 341, cited by Hirsch, p. 182) wrote: "Wet summers are sickly and dry summers are healthy," . . . "except in the neighborhood of marshes, ponds and rivers." The prevalence of malaria in wet years has been observed in many places. (See further, Hirsch, p. 182. This author, by the way, makes no mention of the mosquito-malaria theory. [See also, Laveran[303] (1898), p. 28].) In rainy years there would be a better opportunity for the multiplication of mosquitoes, more pools being formed.

2. *Malarial Country.*—Low, moist places, swamps, jungles, the low seaboard and river estuaries and valleys, especially after inundations have subsided (the Nile, Indus, Euphrates, Ganges and Mississippi valleys, etc.) are the chief localities affected. (Hirsch, Laveran, 1898, etc.) Mosquitoes abound in such places and require pools or almost stagnant bodies of water in which to multiply. Malaria is most abundant as we approach the equator, where insects are also most numerous throughout the year.[1] In countries where irrigation has been introduced without regard to efficient drainage, an outbreak of malaria, or an increase in the severity of the cases, has followed. We have an example in Southern California. (Welch and Thayer[292], 1897, p. 97. Hirsch also refers to such cases.)

3. *Conditions which afford protection against malaria—and mosquitoes.*

Protection of the body. That *closing the windows and doors at night*, as well as *the use of mosquito-nets, gauze veils, curtains, etc.*, protect against malaria is a matter of long experience in malarious countries. Johnson[269] (1818), Macculloch[270] (1827), Brocchi cited by Goode[272] (1834) and Evans[271] (1837) refer to the protection afforded by the use of gauze or fine cloth at night. Macculloch writes that by surrounding the head with a gauze veil or canopeum, the action of malaria is prevented, and that it is even possible to sleep in the most pernicious parts of Italy without hazard of fever. Day advises the use of mosquito curtains "through which malaria can seldom or never pass." Oldham[274] (1871) states that the

[1] The fact that malaria does not occur in northern countries, where mosquitoes are also at times found in great numbers, may be due to the low temperature there, hindering the development of the malarial parasite in the body of the insect. Besides that, the northern species of mosquitoes may be unsuitable hosts.

Jeevas of the Punjaub, who are employed in fishing and catching wild fowl, spend the whole night in their boats, under the reeds of the marshes, "unharmed in the midst of malaria;" but they are wrapped from "head to foot" in a peculiar custume that completely envelopes them, and which they always put on at sunset; and, moreover, a smouldering fire is kept up in the boat. (Quoted from King.) Bignami[289] (1896) states, as we all know, that the inhabitants of malarial districts avoid going out at night or sleeping in the open air. They close their windows and doors tight and use mosquito bars. He writes that it is known that *covering the skin* is a protection, and relates the case of a Russian physician who had never acquired malaria in malarial countries, because he always slept with gloves and a mask. He states that Emin Pasha always took mosquito-nets with him on his African journeys, considering that they kept off malaria, and he cites Nicolas ("Hygiene of Camps and Marshy places") as writing, "Without attributing to the puncture of mosquitoes any relation whatever with the microbes of the fever, one may be certain that irritation by them produces sleeplessness and predisposes to fever." Quite recently Koch[298 300] (1898) has come forward in favor of the mosquito-malaria theory and advises the use of mosquito-nets, screens, curtains, and clothing which is impenetrable to the proboscis of the mosquito, as well as quinine as a prophylactic measure. King[278] (1883) recommended all of these.

Agglomerations of Houses exclude Malaria.—Malaria does not penetrate into cities situated in malarial districts, because the mosquitoes are stopped by walls, hedges, etc., and are attracted by the lights in the suburbs. The mosquito-malaria theory offers an explanation as to why people living on one side of the road are attacked by malaria, while those on the other side escape, "as on the High Road between Chatham and Feversham" (Macculloch[270]). The same thing has been observed in Cività Vecchia (Johnson, references cited from King). Jilek ("Ueber die Ursache der Malaria in Pola" Wien, 1868, referred to by Hirsch) showed that especially those parts of the town of Pola, which were most exposed to the winds from the neighboring swamps were affected by malaria. Wilcocks (American Journ. of the Med. Sc., Jan., 1847, Hirsch) observed in the severe malaria epidemic which visited Philadelphia in 1846, that the disease affected almost

exclusively persons who lived in streets or rows of houses exposed to the south wind. Laveran[287] (1896) cites Mendini as saying that the central parts of Rome are healthy because they are free from mosquitoes. During the malarial season only those persons who venture out of the city walls acquire malaria (Laveran[303] (1898) p. 9).

Protection afforded by intervening Woods or Expanses of Water. —Woods have the power of obstructing or preventing the transmission of malaria by the wind. In other words, they hold back the mosquitoes that are blown or fly there from a malarial foyer. This has been best demonstrated by the influences denudation and planting have had upon the health of communities. Coons (Transylvanian Journ. of Med., II, p. 112, Hirsch, p. 208) reports the following regarding the malaria epidemic of 1826 in Alabama: In the vicinity of Moulton, and situated half a mile from a swampy lake, was a large farm on which all the people had previously been healthy. A thick wood, which lay between the lake and the farm, was cut down. This wood had hitherto served as a barrier to the winds coming from the lake. Of 150 persons living on the farm only 3 or 4 escaped the malarial infection. Wooten (Lewis, Med. Hist. of Alabama, p. 17) reports a similar case, that of a plantation which was separated by a dense wood from a creek which flowed between swampy banks, and was situated about a quarter of a mile away. In the winter of 1842 to 1843 the wood was cut down, with the result that already in the following summer the negroes on the plantation who had previously been healthy, were severely visited by malaria. The owner of the plantation was compelled to transfer the negroes to the other side of the creek, the bank on that side being separated from the new settlement by a wood. The result was that the cases of malaria decreased and people living on that site remained healthy. Sir Francis Day (cited by King) wrote: "Malaria may be carried by the winds to places where it was not generated; it is obstructed by and hangs in the foliage of trees, *or in mosquito curtains;* it subsides into low places, and may be blown over a hill, and may be very virulent on the side opposite to that on which it was formed. In like manner it may be taken up the side of a hill, and, as a lull takes place in the atmosphere, consequent upon its weight it rolls down, and may thus envelope its base with a deadly belt of fever, for there, hanging in

the leaves of the trees, it gradually sinks through them to the earth beneath, in which situation it is most dangerous to pass the night. Mondineau (" La pathologie et l'hygiène des Landes," Paris, 1867, Hirsch, p. 209) writes: " One thing is certain, that in the wastes of the Canton of Houielles intermittent fevers have become much rarer, and especially much milder, since great forests of pines have come to form a natural barrier to the propagation of the miasma." Dods[276] (1878) says he has never noticed that persons living in the vicinity of rank vegetation suffer particularly from malaria as long as the growth is left undisturbed. He notes the unhealthiness of the Assam tea-gardens when the virgin forest is first cleared away. It is the *clearings* in Borneo forests that are unsafe, protection being afforded by keeping in the forest to the windward of the clearings. He advises when the soil is turned to scatter lime on it or if possible to beat it down and cover it with turf. It is needless to multiply the references to the literature on the subject, or to dwell on the fact that the planting of trees also modifies the drainage and moisture of the soil. (See also Appendix.)

Bodies of water lying in the course of winds coming from a malarial center are known to be protective. Ships anchored off a malarial shore where the wind is blowing from the land, remain free from malaria unless they get quite close in, and even then the cases of infection are rare.

Sir John Pringle (" Observations on the Diseases of the Army in Camp and Garrison," London, 1752, cited by Laveran) states that the British army in Holland in 1747 suffered so severely from malaria that some battalions could only muster a seventh of their men. The squadron anchored in a canal between Zuit-Beveland and the Island of Walcheren was quite free from fever.

Blane (" Observations on the Diseases incident to Seamen," London, 1799, p. 221, cited by Hirsch, p. 209) wrote: " When the ships anchored at Rock Fort, they found that if they anchored close to the shore, so as to smell the land air, the health of the men was affected, but upon removing two cables' length,[1] no inconvenience was perceived." Rattray (Edinburgh Med. Journ., 1859, Feb., pp. 708, 710, Hirsch) made similar observations on ships lying in Hong Kong harbor: " The fever, . . . while fatally prevalent

[1] A cable measures 120 fathoms. Two cables would represent an increase of 480 yards in the distance of the ship from shore.

on shore, the ships in the harbor, even when lying at very short distances from the shore, are usually or often exempt from its ravages." Vincent and Burot ("Le paludisme à Madagascar," Rev. sc. 18 juilliet, 1896, et Acad. de méd. 7 avril, 1896) write that the most of the soldiers in the Madagascar expedition acquired malaria whilst the sailors on men-of-war or merchant ships, in spite of great fatigue, remained unaffected. Some vessels remained as long as six months at the anchorage of Majunga, scarely 300 meters distant from the shore, but none of the men, with the exception of those who were sent up the river and were obliged to sleep on the ground, acquired fever.

This indicates that the infectious agent is heavy and must gravitate into the water. Now we can readily imagine that mosquitoes, which are not capable of maintaining a prolonged flight, fall on to the water, and, especially if it is agitated, may not be able to rise again. Besides, if they rise it would rarely be to the height of a ship's deck. Assuming that the mosquito is the carrier of the infection, we can understand how the wind passing over land would carry the infection further than on water, for the mosquito would rise (this occurs especially during the lulls in the wind) and fall continuously in one direction, being able to rest occasionally, his powers of further flight being unimpeded. I have often, and others have also, no doubt seen insects rise and fall this way in the air, always being carried some distance in the direction of the air current. The flight of the mosquito being usually close to the ground, and its frequently having to stop and rest by clinging to the vegetation, would account for the insect being usually transported but to a limited distance, and explains how the woods serve as sieves to the "malarial poison." (When the wind is blowing strongly, mosquitoes are no longer troublesome, because they seek shelter and cling to the vegetation.)

Cultivation of the soil has hundreds of times been observed to rid a district of malaria. (Hirsch cites a number of cases, p. 193; see also Laveran (1898). As King and others have observed, this is probably due to the swamps and pools, the "mosquito-nurseries" being drained and removed. I should add that a change in the character of the vegetation might also be considered a factor in relation to these insects.

Flooding the Land.—The complete flooding of pools, ditches and

marshy land has proved as effective as draining the land and cultivating it. (Hirsch, p. 193), Dods[276] (1878), who spent 20 years in the tropics, had never seen malaria particularly prevalent in the rice fields as long as they were *covered* with water, it is only when the crops are cut and the rice-fields begin to dry up that they are dangerous. Laveran (1898, p. 31) cites Boileau-Castelnau (1850) as stating that rice-fields are healthy when the water circulates, but the reverse when it stagnates.

The Avoidance of Sleeping out-of-doors at Night, or of Exposure after Sunset.—It is notorious that malaria is most dangerous when the sun is down, whereas it seems relatively inert during the daytime (Laveran (1898), etc.). King writes, "With regard to the mosquito, however, it is well known that it remains, for the most part, during the day, harbored in woods, weeds or low underbrush, and comes out after sunset and at night to indulge its blood-sucking proclivities." It is well known that *sleeping* out-of-doors after sunset is more dangerous than waking, "for it is undoubtedly true," writes King, "that while awake, the person exposed will move about, or brush away the insect, while he will submit to be bitten during sleep." Bignami[289] makes the same statement.

The Use of Fires.—King writes, "In malarial districts, the use of fire, both in-doors and to those who sleep out, affords a comparative security against malarial disease." . . . The mosquito "is well known to be attracted by lamps, lights and fires into which it heedlessly flies at the cost of its life." . . "Every fire therefore, whether in-doors or out is a sort of mosquito hades. In some tropical countries despite of heat of climate, fires are kept up all night in every apartment as a preventive against fevers; and experience has demonstrated that they are more effective when placed between the open window (or door) and the body of the person to be protected. In this way it is easy to comprehend how every mosquito will fly directly into the light and the fire before reaching the thus protected sleeper." The smoke itself would also drive away insects. Bignami[289] (1896) says that those persons in the Roman Campagna who sleep in shepherd's tents (which are cone-shaped, with a fire in the middle of the floor and an escape for the smoke at the top—the atmosphere in the interior being very smoky) do not acquire malaria. I have already referred to the fires used by the fishermen in the Punjaub. I should say that the ascensional

currents of air produced by fires will also carry many mosquitoes away.

Immunity of Persons working in Sulphur mines, Fumigation said to afford protection.—d'Abbadie[277 284] (1882) states that the native elephant hunters in Ethiopia who reside on high plateaus where the climate is relatively cool venture unmolested into the hottest and most malarious districts. "*They attribute this immunity to their habit of subjecting themselves every day to fumigations of sulphur*," the naked person being exposed to the fumes.

d'Abbadie mentions investigations made by Prof. Silvestri of Catania, in Sicily, which showed that the workmen in sulphur deposits ("soufrières"), situated at low levels in malarial foyers, were relatively exempt from fever. Whilst 8 to 9 per cent of the sulphur-workers were malarious, as many as 90 per cent of the population in the vicinity who followed other occupations suffered from malaria. Fouqué had also informed him regarding the now uninhabited Zephyria near Milo, in Greece. This city had at one time a population of 40,000 inhabitants, but malaria gradually exterminated the inhabitants. It is impossible to pass the night there now without acquiring malaria. The depopulation of Zephyria seems to have begun about the time when the sulphur deposits thereabouts ceased to be worked. Fouqué also wrote that there are sulphur works on the western border of the malarious marshy plain of Catania. Situated near the sulphur works but on a higher level are the remains of a village which had to be abandoned at the beginning of this century on account of malaria. A colony of workmen reside at the sulphur works whilst the village above remains uninhabited.

I do not know if similar observations have been made elsewhere. If it is true that fumigation with sulphur protects against malaria we would have another fact to support the mosquito hypothesis, for the smell of sulphur would repel these insects. It seems to me that the matter decidedly deserves further attention. On the other hand mosquitoes would scarcely find a suitable place in which to multiply in localities where the soil is permeated by sulphurous emanations.[1]

[1] Whilst in Rome in March Professor Grassi showed me a letter from an Italian gentleman which stated that fumigation of the body with sulphur is used in Italy to-day as a safeguard against mosquitoes.

Racial Immunity.—The relative immunity exhibited by the negro race towards malaria[1] is due, King thinks, to protective coloring. Besides many negroes anoint their bodies with grease, whilst others emit an offensive odor from their persons—one or more of these factors may serve to some extent to keep off mosquitoes.[2] Laveran (1896), states that delicate-skinned people and children are more susceptible to malarial infection because they are more readily bitten by mosquitoes. Laveran (1898, p. 124), attributes the immunity of the negros to their thicker skin, and states they are less subject to mosquito bites.

4. *Influence of Occupation.*—"The occupation has much to do with susceptibility to the disease," write Welch and Thayer[292] (1897) "soldiers and tramps who sleep upon the ground in malarious districts are particularly susceptible. Fishermen in the bays and inlets along the southern shores of the United States, as well as farmers and berry-pickers in the same regions, are particularly open to infection." "Furthermore," writes King, "in certain districts where the so-called 'malarial poison' is supposed to be lodged in trees and bushy plants near the ground, it has been observed that those persons are particularly prone to fever who cut down and disturb these malaria-laden plants, which is extremely suggestive of the mosquitoes being disturbed from their reposing haunts, just as one might get stung by stirring up a bee-tree or a hornets' nest.

[1] See authorities quoted by Hirsch (p. 172). Thayer and Hewetson's (Malarial Fevers of Baltimore, Johns Hopkins Hosp. Rep., 1895, vol. v) figures indicate that the negro is only about one-third as susceptible as the white man. See also cases cited by Laveran (1898, p. 113).

[2] That insects are particularly sensitive to certain odors is a matter of wide experience. Whilst the odors of flowers attract some, they repel others, and the same thing may be observed with regard to animals and blood-sucking insects. Fleas (*Pulex irritans*) are repelled by the smell of the horse, and stablemen are protected by the odor they acquire. Railliet[242] in fact advises the use of a horse blanket for the purpose of driving off fleas. The bed-bug is attracted by the smell of the human subject, especially by certain individuals, whilst others perhaps lying in the same bed are not bitten. It is a matter of common experience that some persons are more subject to the attacks of mosquitoes than others. King[278] (1883) advises the use for prophylactic purposes (against malaria) of some terebinthinate, camphorated or eucalyptolized ointment or liniment, the use of smoke, etc. Koch[298 300] (1898) does the same. Either garlic or camphor, placed in a bag and carried on the person, was considered, as Lind (1779) states, a prophylactic against malaria in the last century, and Laveran[303] (1898, p. 124) relates that the tradition exists in Italy and France that fevers are avoided by eating garlic.

La Roche, in his well-known work (p. 282) says: 'Malaria is collected by plants, particularly on cutting them down or rooting them up, thus exciting fever in the laborers who might otherwise have escaped, as proved by the circumstance that in all these situations, while the workmen are in the erect posture and engaged at their work, they escape the fever, but are attacked if they sit, and more particularly if they lie down on the ground—and that whether they sleep or not.' Macculloch[270] (p. 124) says of the Roman Campagna 'if the laborers cut down certain plants (a bushy thistle chiefly), a fever that would otherwise not have occurred, is the consequence.'"

5. *Effect of turning up the Soil.*—Malaria may develop in previously healthy districts in consequence of digging the beds of canals, railway tracks, foundations for houses, etc. A severe outbreak of malaria was associated with the excavation of the Panama Canal, and malaria also followed the excavation of the canal St. Martin and the fortifications of Paris. The same has been experienced many times over in various countries (Hirsch, Welch and Thayer, etc.). It is probable in such cases that pools of water are formed in the excavated land, thus giving rise to mosquito nurseries, and it is possible that these become infected by workmen coming from malarious districts. Moore (Indian Med. Record, 16 Dec., 1897), believes that it is a mistake to speak of malaria being caused by "soil disturbance," he says he has always found that there has been an interference with subsoil drainage resulting in "a marsh or allied condition."

Elevation in Relation to Malaria.—It is well known that only living in the upper stories of a house in a malarial district affords protection. Osler (Pract. of Med., p. 142, New York, 1892) writes, "Persons dwelling in the upper stories, or in buildings elevated some distance above the ground, are exempt in a marked degree." Laveran and others make similar statements. As King puts it, malaria "hugs" or "loves the ground." Sleeping on the ground is particularly dangerous because we are then more exposed to the bites of mosquitoes. Laveran cites as examples of the effect of elevation, that at Constantine (Algeria), the mosquitoes are very numerous in the valley of the Rummel, which is malarious, but that they disappear as we go into the more elevated parts of the town, which are healthy. The same has been observed at Bone. Le

Gendre (Étude, sur la topographie médicale du Médoc, Paris, 1866, p. 26, cited by Hirsch) states that the zone of hills in the province of Médoc is only visited by malaria when the winds blow their way from the neighboring swamps. Cornay (Topogr. méd. de Rochefort, Paris, 1845) and Crouigneau (Réc. de mém. de méd. milit., vol. LXII) both report similar observations in Rochefort and Rochelle. Russell (Address, New York Public Health Association, 1876, cited by King) states that under ordinary circumstances, a certain altitude affords immunity, although low elevations of 200 to 300 feet above a miasmatic tract are often more dangerous than the flat lands, the poison seeming to float upward and become intensified. This he adds has long been noticed on the heights of Bergen Hill, West Hoboken and Weehawken which overlook the Jersey flats. The mosquito, King remarks "can readily be understood to be 'obstructed' and 'accumulated' by forests on the brows of hills, etc.," having been blown there by the wind. Koch (1898) writing of malaria in German East Africa states that this disease is not found there at an elevation of over 1200 meters, a point at which mosquitoes also disappear. It is needless to multiply examples for the above observations have been made repeatedly.

The elevation at which malaria occurs is influenced by the average temperature prevailing at the place during the summer. This elevation naturally increases as we approach the equator. The freedom of the mountains from malaria is chiefly due to more perfect drainage. Where malaria does occur in the mountains it is always in valleys exhibiting but a slight fall or in depressed imperfectly drained areas situated on the high plateaus. (Hirsch.)

6. *The Rôle of Insects and Ticks in other Haematozoal Diseases.*—Laveran[287] (1896), Bignami[289] (1896), Welch and Thayer[292] (1897) and Koch (1898) have all brought out in support of the mosquito-malarial theory the evidence that ticks have been proved to reproduce Texas fever in cattle (see Texas fever), and that mosquitoes have been shown to be intermediary hosts to the *Filaria sanguinis hominis* (see Filariasis). The rôle of the dog-flea in relation to *Filaria recondita* of the dog is also suggestive. We have seen that young ticks may harbor and transmit the infectious agent of Texas fever to cattle and it is just as possible that the malarial parasite may be transmitted to the young mosquito; and if it is transmitted to one generation, it may continue to be transmitted

from mosquito to mosquito, thus maintaining its existence in nature. (See *Grassi's* views below.)

7. *The Coincidence of Malaria and Mosquitoes.*—Wherever we find malaria we find mosquitoes, but wherever we find mosquitoes we do not of necessity find malaria. As King puts it, all mosquitoes will not produce malaria any more than the scratch of every lancet will produce vaccinia, or the bite of every dog hydrophobia. The filarial diseases above-named, as also Texas fever, are also not found in all places where there are mosquitoes, fleas and ticks.[1] Lind[268] (1757-1762) tells of an army, half of which was lost whilst passing through Hungary, "The air swarmed with insects—a sure sign of its malignancy"; and, referring to the climate of Guinea, the East and West Indies as being fatal to Europeans "more especially when molested with heat within-doors, and the plague of mosquitoes, they have ventured to sleep in the open night air." Laveran[287] (1896) states that the French soldiers on the Madagascar expedition of 1895 suffered very much from malaria, and that they were "assaillis par des legions de moustiques." According to Manson[284, 290] (1896) mosquitoes abound in Mauritius and Réunion where malaria prevails. Ross[296] (1898, II) made interesting observations in this connection in the very malarious Sigúr Ghât or Cañon leading from the Ootacamund to the Mysore plateau. Malaria commences 3 miles down the ghât, at a height of 5500 feet above sea-

[1] Stebbins[270] (1884), who criticises King's paper, considers that he has established its inaccuracy by the statement that he has been in various places where mosquitoes swarmed, but there was no malaria. Nicolas[279a] (1889) (I am indebted to the great kindness of Prof. Laveran for this extract) also considers the absence of malaria in the presence of mosquitoes is a ground against the acceptance of the theory. He writes, "En résumé le moustique est souvent le compagnon du virus malarien, mais ce dernier peut se passer de son concours," to which Laveran remarks in a letter to the writer: "En somme Nicolas n'apporte aucun fait personnel à l'étude de la question." Hammond[118] (1886) knows of no locality subject to malaria which is not infected by mosquitoes. Ziemann[301] (1898) does not express himself in favor of the mosquito-malaria theory, he writes: "Kamerun, one of the worst fever centers on earth, is further but slightly affected with the plague of biting insects. (So there are mosquitoes there also. N.) During our stay on the western coast of Africa, I only once experienced a real mosquito plague; this was on the so-called Bimbia-Creek, north of the Kamerun river, cases of malaria having already occurred before. It is known on the West African coast that every 4 to 5 years a particularly severe year for fever occurs. I never heard that in such years a marked mosquito plague was noted."

level. At the bottom of the ghât 80 per cent of the people examined had enlarged spleens, and mosquitoes were very plentiful at that point, " being bred in a puddle lying within a few yards of the bungalow and of an irrigation pool, from which the servants drew their drinking water. Further down the ghât, however, and for its whole length, I did not succeed in finding a single mosquito grub in any of the pools of the ghât river or its tributaries, nor did I find a single one at Mr. Nash's plantation, where fever was prevalent." At first Ross was inclined to give up the mosquito hypothesis. " I was, however, saved from this conclusion by the discovery that, though larvæ could not be found in the ordinary sources of drinking water, the whole jungle abounded with fully-developed mosquitoes to such an extent that it sufficed to sit down in the wood at noon to be surrounded by numbers of a virulent but small species of the insect," to which he gives the provisional name of *Culex silvestris*. This mosquito " appears to live entirely in jungle and undergrowth, especially in shady parts, and seldom, except perhaps at night, enters dwellings. Another remarkable difference in habits is that, while the ordinary species never travels far from pots and puddles containing stagnant water, the *silvestris* may, in my experience, be seen fully half a mile away from any water. Indeed I found it a matter of considerable difficulty to discover the larvæ at all . . . in a few scanty puddles at the bottom of nearly dried up and dark nullahs." One of his servants who was employed in catching the adult mosquitoes " by allowing them to settle on his legs and arms, was attacked 5 days afterwards by the quartan parasite."

Joly[137] (1898, p. 44-50) considers that the evidence in favor of the transmission of malaria through the bites of infected mosquitoes is stronger or at least equal to that presented on behalf of the theory of its transmission by water. He reports the case of a friend who spent two days in shooting in the marshes near the Etang Blanc near Tosse (Landes) where malaria prevails. The party to which he belonged took their food and drink with them, and avoided drinking any water in the infected district. Mosquitoes abounded, his friend was severely bitten by them, and eight days later, whilst in Paris, he developed typical malaria. He had never been in a malarious district before, nor had he ever previously had malaria. The infection through water being excluded, Joly con-

siders that the mosquitoes are most probably to be regarded as having inoculated the disease. Joly also states in this connection that malaria is endemic on the borders of the pond of Cazau, several persons having acquired malaria there who came from Bordeaux. The water of the pond (étang) is used for drinking purposes. The downs in the surrounding forest contain many mosquitoes. Persons who traverse the downs or work in the adjoining woods are much troubled by these insects and nearly all who reside thereabouts acquire malaria. The water supply of Arcachon has been derived from the pond at Cazau for the last 3 years, but no malaria has occurred there. It is evident that if the water were the source of infection at Cazau it would be the same at Arcachon, but this is not the case. At Arcachon there are no marshes and mosquitoes are relatively rare. Joly considers that malaria may be communicated by mosquitoes which have acquired the infectious agent in malarial swamps, as also, but more rarely, by mosquitoes which have previously bitten a malarial subject. He also believes that infection may occur through water which may or may not have been infected by mosquitoes.

Koch[298] (1898, I) says that he has never seen malarial in places where there are no mosquitoes. He states that malaria does not occur on some small East African islands, for instance at Chole, which lies south of Mafia. "It was surely not an accident," Koch writes, "that this should be the only place on the coast where I found no mosquitoes and required no mosquito-net."

8. *Mode of Infection.*—Under natural conditions malarial infection must occur through the agency of air or water. There is no clearly positive evidence that malaria may be conveyed by water, and all experiments hitherto made have given negative results. Some observations (Laveran, 1898, p. 118), however, do suggest the possibility of this mode of infection. Manson, and also Laveran, believe that man may become infected by drinking water in which mosquitoes previously fed on malarial blood have died. They also believe that infection may occur through the inhalation of dust arising from dried pools which have harbored the parasite. This conception is based on Manson's observations in connection with *Filaria*, and of course the possibility of this mode of infection cannot, in the present state of our knowledge, be denied. A number of authors recommend the boiling of drinking-water as a prophy-

lactic measure. On the other hand King, Laveran (also), Bignami, Mendini, Koch and others believe infection occurs through the bite of the mosquito; Manson believes that this is only exceptionally the case. The writer believes it is the rule in view of the evidence above given and that about to be presented below. The view that the mosquito carries the infection directly from man to man is untenable, according to (Laveran, Koch), for if this were the case infection would be much more frequent. Though the disease is inoculable from man to man and man to monkey subcutaneously, the quantity of blood inoculated has to be a considerable amount—far larger than it would be possible for mosquitoes to remove or reinoculate, supposing that they were capable (and that seems to me impossible) of inoculating by the simple introduction of an infected proboscis.[1]

9. *The Malarial Parasite outside the Human Body.*—If we accept the mosquito-malaria theory at all, we are forced to the conclusion that the mosquito must be the *intermediary host* of the malarial parasite. If the insect gives rise to malaria through its bite, then *the parasite must be given off in the mosquito's salivary secretion* when it is sucking blood. (I had come to this conclusion when the remarkable observation just published by Ross (1898) below referred to came to give the supposition the much needed experimental support.) Knowing that malaria may be acquired in regions very rarely visited by man, we must regard the latter as but an occasional host of the parasite in nature. It remains then to be proved whether the parasite is capable of living an independent existence, or if it is always a parasite living on the mosquito or some other host besides man. Manson, Ross, Bignami and others have expressed the opinion that the mosquito is the intermediary host of the malarial parasite of man. Bignami holds the opinion that the mosquito may become infected by the malarial parasite during its development in damp soil, and, that the malarial germ may be primarily a parasite of the mosquito which by its bite causes malaria in man.

Both Manson[288 290] and Laveran[287] (1896) express the belief *that man may introduce malaria into a country by infecting the mosquitoes*, the disease becoming endemic. Lacaze (Union méd., 1872,

[1] The experiments of Ross and of Grassi, cited below, have been published since the above was written.

No. 116, Hirsch, I, p. 211) states that malaria had existed for about three years in Mauritius when the first cases began to occur in the island of Réunion. "Ici l'importation a eu lieu par Maurice, selon une probabilité qui touche à la certitude." Manson says mosquitoes abound in Mauritius and Réunion and that now one-third of the deaths there are due to malaria.

Experimental Evidence in Relation to the Mosquito-malaria Theory.

Acting upon a suggestion of Manson's, whose researches on *Filaria sanguinis hominis* had shown the mosquito to be an intermediary host of this parasite, Ross[285] (1895) in India, exposed malarial subjects exhibiting crescentic parasites in their blood, to mosquitoes, and observed the parasites undergoing a metamorphosis within the insect's stomach, similar to that observed on the slide in malarial blood taken directly from the malarial subject. Ross and also Manson, held the opinion (since modified) that the flagellate bodies penetrate into the host, *i. e.* the mosquito. Whilst examining some mosquito larvæ at Secunderabad (Deccan) Ross observed gregarines[1] in their stomachs, and concluded that they might represent stages in the development of the malarial parasite. Manson and Laveran naturally considered this conclusion as premature, though Manson[288 290] (1896) believed that the observations supported his theory of the life history of the malarial parasite. Ross "tracked the germs of this gregarine into the stomach of the mosquito larva, where after an intracellular stage of short duration, and which was not quite satisfactorily made out, it became a large, free, actively-moving gregarine." At maturity they wandered out of the stomach into the Malpighian tubes, crept to the cœcal end and became encapsuled. Pseudo navicellæ were then formed within the capsule. When the insect has attained the nympha stage, or is fully developed, the capsule ruptures and the pseudo navicellæ escape in great numbers, being given off in the fæces. This was observed in the fully-developed insect whilst in the act of sucking blood. As the mosquito larva devours its own and its neighbors' exuviæ it is easily understood how all the mosquitoes in a pool may become

[1] Ross subsequently[296] (1898, II) found similar parasites in mosquitoes at Sigûr, also several other protozoal parasites "any one of which may just possibly be a dimorphic form of the malaria parasite."

infected, and the flying insect might spread the infection from pool to pool. Manson thought this might indicate the mode by which the malarial parasite completes its cycle. At any rate these observations stimulated Ross to continue his studies.[1]

Manson[288] (1896, Lancet I, 751) elaborated his theory as follows: He wrote "as the plasmodium is a passive blood parasite, its escape from the body might be effected on the same principle that the escape of the passive muscle parasites effected. As the latter obtain their opportunity by being swallowed by some flesh-eater—some carnivorous animal—I thought the former might get its chance of development by being swallowed by some blood-eater, some suctorial animal, such as the flea, the bug, the louse, the leech, the sand-fly, or the mosquito." The same idea had already been expressed by Laveran. Manson further drew an analogy between the malarial parasite and the filaria. The filaria is enclosed in a sheath when in the blood, the malarial crescentic parasite is enclosed within the red blood corpuscle, and both parasites when removed from the body leave their enclosing envelope and become motile. This occurs both on the slide and in the stomach of the mosquito. The filaria having cast its sheath, leaves the digestive tract of the mosquito and bores its way into the thoracic muscles where it completes its metamorphosis. Manson believes that something similar may occur with the malarial parasite, the latter becoming a parasite of the mosquito and entering some cell after the manner of a gregarine or coccidium. The female mosquito having filled herself with infected blood, in due time lays her eggs and dies, her body floating in the water near the egg-raft. The larvæ on escaping from the egg often eat up the dead mother and thus in turn become infected. Manson believed that the malarial parasite may enter the human body through the medium of drinking water, or be inhaled as dust originating from drying up of mosquito-haunted pools, the parasite being in the resting stage. He suggests that the

[1] Wishing to determine if water might serve as a vehicle for the transmission of malaria to man, Ross allowed mosquitoes to fill themselves with malarial blood, and placed them so that they laid their eggs in the water and died there. The water, containing the eggs and grubs of these mosquitoes, was given to several natives in quantities of 1 to 2 drachms. Eleven days later one patient developed a malaria, which lasted 3 days, during which time he exhibited the parasites in his blood. Of course no value can be attached to this single experiment.

soil may become infected by mosquitoes falling and dying in it. According to Manson then, the mosquito does not produce infection by its bite, but simply serves as an intermediary host which contaminates the water or soil with resistant forms of the parasite after the latter have undergone a certain metamorphosis in the insect.

Bignami[289] (1896) tried together with Dionisi (1893-1894) to determine if mosquitoes were capable of producing malaria by their bites.[1] For this purpose they liberated mosquitoes, gathered on malarial ground near Rome, in a room in which they placed a healthy man. They made two experiments, both of which proved negative, a fact which they attributed to the dispersion of the mosquitoes in the room and the experiment not being kept up long enough. Bignami states that Calandruccio had observed the malarial parasite to die off both in the stomach of the mosquito and that of the leech. He gives a few of the reasons, given by me in the preceding pages, for his belief that the mosquito inoculates man directly with malaria.

Ross[293] (1897) having continued his observation on mosquitoes reported that after examining a very large number of these insects he had finally succeeded in finding a few belonging to a particular species[2] which, after being fed on malarial blood (containing crescents), exhibited certain peculiarities. If he allowed 4 to 5 days to elapse after the mosquito had ingested malarial blood, he observed peculiar pigmented cells occurring in the stomach wall of the insect. These cells measured 12 to 16 μ and could be very clearly differentiated from the tissues of the insect. The fact that these cells contained pigment similar to that of the malarial parasite, and that they were not found in control mosquitoes, was certainly highly suggestive. Though, as Ross states, he had previously examined over a thousand mosquitoes with negative result, this positive, or at least suggestive finding, might be explained on the supposition, *that he had at last found the right species of mosquito to serve as a host for the malarial parasite.* Manson had already expressed the opinion that each hæmatozoön probably requires a particular species of mosquito just as in the case of filaria. The cells found by Ross

[1] Grassi[307b] (1898, II, p. 237) says these experiments were made with *Culex pipiens. Culex hortensis* may also have been used. This would account for the negative result. See further below.

[2] A description of the species will be found in Ross's article, as also figures of the pigmented cells in the mosquitoes' stomachs.

in the stomach wall of the mosquito contained a number of stationary vacuoles, no contractile vacuole, no amœboid or intracellular movements and apparently no nucleus. All the cells contained pigment granules similar to those of the malarial parasite, the granules, 10 to 20 in number, being either bunched together or distributed in lines disposed diametrically or peripherally as in certain hæmatozoa. Some of the granules exhibited slight oscillation. In one mosquito examined after 4 days, 12 such cells were counted in the stomach wall; in another examined after 5 days, there were 21 cells, but these were more sharply defined and larger than the others. Ross was cautious in drawing any definite conclusions from his work in view of the small number of his observations, the latter however, gave his subsequent experimental researches a definite direction. Ross's specimens were sent to Manson in London and examined by him, as well as Sutton and Thin. In a publication which appeared shortly after the above, Ross[295] (1898, I) expressed the belief that the pigmented cells in the mosquito's stomach wall must be pathological growths, and did not doubt that they were malarial parasites. Ross states that he examined some scores of "dappled winged" mosquitoes unfed or fed with healthy blood; all the examinations were negative, until "at last two of this species were persuaded to feed on a patient with crescents. One of them was killed next day; no pigmented cells could be found. The second was killed 48 hours after feeding; numerous pigmented cells were present. They were all small, much smaller than epithelial cells, ovoid, about 7 μ in the major axis, and each contained about 20 granules of typical pigment which were often arranged circumferentially, just as in the malarial parasite." He also records another observation: "a hundred or more grey or 'barred-back' mosquitoes, unfed or fed on healthy or crescent blood, have been dissected without finding the pigment cells. At last one was observed feeding on a patient whose blood that morning had been seen to contain numerous mild tertian parasites." The mosquito killed on the third day contained many pigmented cells measuring 8 to 25 μ. Manson had supposed that the flagellated malarial parasite developed in the stomach of the mosquito might, after the manner of the filaria, gain access to the tissues of the insect. After Ross's publication Manson[294] (1898, I) wrote: "as the flagellum carries no pigment, if the pigmented cells belong to the mosquito, or

extracorporeal, phase of the malaria parasite, how account for the pigment these cells contain?" He considers that MacCallum's recent discovery (Journ. of Experimental Medicine, 7 Jan., 1898) apparently supplies the explanation. MacCallum found in the case of halteridium infection in birds as also in the æstivo-autumnal malarial parasite of man, that the function of the flagellum is to impregnate the pigmented spheres. In the case of halteridium [1] the impregnated spheres after a short period of rest became converted into locomotive vermicules which carried the characteristic pigment granules at one end, whilst with the other hyaline extremity they are capable of penetrating and destroying leucocytes, and apparently by the slightest contact to injure the envelope of the red blood cells, so that these exude their contents into the surrounding serum. MacCallum was not able to observe the formation of vermicules in the malarial parasite of man. Manson, however, believes that such vermicules are formed by the malarial parasite in the body of the mosquito, and that the vermicules wander into the stomach wall of the insect, giving rise to the pigmented cells observed by Ross. The latter[297] (1898, III) working in Calcutta at a season unsuited for the satisfactory study of the subject on human malaria, turned his attention to the study of halteridium, and especially the proteosoma (Labbé) infection occurring in sparrows, larks and crows. He observed that—

"(1). Pigmented cells are found in the stomach wall of grey mosquitoes fed on crows, larks and sparrows with proteosoma.

"(2). Pigmented cells are not found in control grey mosquitoes fed on healthy men, or men with crescent plasmodia, or healthy sparrows, on crows and larks, or on crows and pigeons with halteridium.

"(3). These pigmented cells are found in the external coat of the stomach, and grow from a size of 6 μ in 30 hrs. to 60 μ at 6 days, and are probably coccidia.

"(4). Successive feeds by the same mosquito on the same bird are followed by fresh crops of young coccidia.

[1] Ross[297] (1898, III) saw the same thing occur in the stomach of "grey mosquitoes." Grassi[307b] (1898, II, p. 235), who examined these mosquitoes, could not distinguish them from *Culex pipiens*. This he considers important as he had been able to determine the fact (1890) that districts which may be healthy for man are at times malarious for birds. This would correspond with the distribution of certain species of mosquito.

"(5). Similar pigmented cells have been found on mosquitoes fed on human gymnosporidia (Labbé)."

Ross took 30 grey mosquitoes from a batch of grubs procured at one time from the same puddle. Ten (*a*) of these mosquitoes were fed on a sparrow in whose blood the proteosoma were exceedingly plentiful; ten (*b*) he fed on a sparrow in whose blood proteosoma was only moderately abundant; and ten (*c*) he fed on a sparrow whose blood contained no proteosoma. He killed the insects after 50 hrs. and made counts of the number of pigmented cells in the stomach wall of each mosquito. These countings were repeated by Manson on the same specimens. They found on an average in 10 mosquito stomachs belonging to group (*a*) 100.8 (Ross), and 108.4 (Manson) pigmented cells. In group (*b*) 29.2 (Ross), and 57.1 (Manson), whilst in group (*c*) no pigmented cells could be found. Ross states that he has made the same observation repeatedly. Manson, referring to Ross's observations, of which he gives a preliminary report, writes that these show " that certain phases of the hæmatozoal intra-corpuscular parasite of man and birds, after entering the stomach of special species of mosquito, pass into the tissues of the stomach wall of the insect, rapidly increase in size, and probably towards the termination of the life of the mosquito, sporulate, and leave the capsule, which, by that time, has formed around them."[1] Whilst in London in the beginning of June Dr. Manson very kindly showed me Ross's preparations, and I must say that they seemed to me more than suggestive. Laveran, who also examined specimens sent to him by Ross, wrote (June 12th, 1898) to Manson, " It appears to me undoubted that the elements discovered by Dr. R. Ross in the stomach of mosquitoes fed on the blood of birds subjects of hæmosporidiosis, are really parasites, and that these parasites represent one of the phases of the evolution of the hæmatozoa. It is probable that it will now be easy to find the extracorporeal form (la forme de résistance) of the parasites in external media. The discovery of Dr. Ross appears to me as to

[1] Manson gives figures of Ross's preparations showing the mosquito's stomach 30 hours after feeding with proteosoma blood, the pigmented cells lying between the somewhat disassociated muscle fibers of the stomach wall. Other figures illustrate the development of the parasites in the mosquito, and a diagram is given, indicating what is known and " Yet to be ascertained of the mosquito phase of certain human and avian plasmodia."

you, to be of great importance; it is a great step forward in the study of the evolution of the hæmatozoön of birds and very probably also in that of the hæmatozoön of malaria. I have shown the preparations to M. Metschnikoff, who shares my opinion." (Already in another paper Manson and also Lewis are stated to have observed that mosquitoes suck the blood of birds and that they may perhaps communicate "malaria" to them.)

In Ross's[297] (1898, III) report published in Calcutta (dated 21st May, 1898) full details of his painstaking experiments will be found.[1] Of 245 "gray mosquitoes" fed on birds with proteosoma 178 (72 per cent) subsequently contained pigmented cells. Of 249 "gray mosquitoes" fed on men with crescents or immature tertian parasites, on birds with halteridium, on healthy sparrows, on birds with *immature* proteosoma, "not one contained a single pigmented cell." Of 81 mosquitoes fed on birds known to contain *ripe* proteosoma 76 (94 per cent) showed pigmented cells. Ross writes (p. 6), "There can be no question, then, that the pigmented cells are derived directly from the proteosoma. We can, however, already go further. The fact that similar cells were not found in control insects of the same species fed on blood containing other gymnosporadia will convince any one acquainted with parasitology that we are not dealing here with any mere physiological absorption of pigment by the stomach cells of the mosquito, but with a vital phenomenon in the life-history of proteosoma, with a remarkable transformation by which the pigmented parasite in the blood of the bird becomes a pigmented parasite of some kind in the stomach tissues of the mosquito." When the mosquitoes were repeatedly fed on proteosoma-blood, a fresh generation of pigmented cells was observed, the parasites of the last feeding being smaller than those at first taken up. The parasites could be seen projecting from the outer surface of the stomach "like warts on a finger." Whereas the earlier forms of the parasites are pigmented, this is no longer

[1] Ross placed the malarial subjects or birds (in cages) he wished to experiment on beneath a mosquito net, and liberated the mosquitoes into the space. After they had filled themselves, the mosquitoes were carefully caught by an assistant entering the net and placing a test tube over each insect. The tube was then closed by a light cotton plug. A few drops of water were placed in the bottom of the tube for the insect to drink and lay their eggs in. The mosquitoes to be kept alive had to be fed on blood every two days. The tubes were changed daily.

the case in the fully-developed individuals. Where the parasites are situated between the muscle fibers of the mosquito stomach Ross observes that they remind one of the trichina, from the fact that they cause a displacement of the muscle fibers.

Koch[298] (1898, I), as stated previously, expresses himself strongly in favor of the mosquito-malarial theory. Strange to say he makes no mention whatever of the publications of Ross and Manson, though he writes that he considers experimental work on the mosquito theory to be of extraordinary importance. He says that "experience has shown that dwellings and sleeping apartments which allow a free passage of air are less to be feared than those in which the air stagnates. It is my conviction that this is due to the latter being preferred by mosquitoes." He, for this reason, recommends the British-Indian bungalow as a model for houses to be erected in the German colonies in Africa.

In a letter dated 7th September, 1898, Dr. Ross gave me further particulars regarding researches then unpublished. He states that in July he had succeeded in producing proteosoma-infection in sparrows, weaver-birds and crows by means of infected mosquitoes. I obtained additional information from Dr. Manson who had likewise received a communication from Ross, the contents of which he reported at a recent meeting of the British Association in Edinburgh. (Manson[302], 1898.) Since the publications already referred to appeared, Ross found that if he crushed the encapsuled *Proteosoma* taken from the mosquito's stomach and placed it in salt solution, that an enormous number of minute spindle-shaped slightly flattened bodies, which he calls "germinal rods," issued from within the capsule. These bodies do not seem to be motile, but they gain access to the body cavity of the insect, and are distributed in all directions by the blood-current, and finally accumulate in vast numbers about the 5th to 6th day after feeding *within the cells of the salivary gland*, the cells of which crammed with the parasites remind Ross of the bacilli-filled lepra-cells. The encysted parasites either give rise to these spindles or to a few "black spores," the significance of which Ross is not prepared to explain. They are not altered if kept for weeks in a moist chamber and do not develop when fed to mosquito grubs. *Ross believes that infection results from the bites of mosquitoes whose salivary glands contain the spindle-shaped bodies.* Of 28 sparrows 22 acquired severe pro-

teosoma infection as the result of being bitten by infected mosquitoes. Of 4 weaver-birds and 2 crows bitten by infected mosquitoes, only a crow remained healthy. Particularly severe infection resulted in 5 sparrows similarly treated, which had previously been affected by a mild infection. The "gray mosquitoes" used for these experiments in India are found in ditches, puddles, etc., up to an elevation of 7000 feet above sea-level, and *this corresponds according to Ross to the distribution of the proteosoma-disease in birds.* The "dapple-winged" mosquito to which he attributes a rôle in human malaria, is only found in small puddles caused by the rains, in which no fish or frogs are found. This would explain, he claims, the distribution of æstivo-autumnal malaria in India and its dependence on the rainy season.

Ross advises in consequence as prophylactic measures against malaria (besides the use of mosquito-nets) that measures be taken against ponds, puddles, cisterns, etc., which serve as mosquito nurseries, especially such as are situated in proximity to dwellings, camps, etc. He suggests that they be drained at short intervals so as to prevent the development of mosquitoes (see Appendix). Ross considers that malaria patients should be kept under mosquito-nets, as, in the presence of the proper species of mosquito, they may lead to the further spread of the disease. In a letter dated 31st October, 1898, from India, Dr. Ross informs me, in answer to some questions I sent him, that his full report will be submitted in January. He also sends me some further details regarding his experiments. "The length of time between infecting a mosquito and its being able to cause infection is presumably about 7 or 8 days, namely, the period it takes the coccidia to mature and the germinal rods to enter the salivary glands;" this question is at present engaging his attention. Birds become infected from 5 to 6 days after being bitten. The number of mosquitoes required to cause infection has still to be determined. The sparrows used for his mosquito-infection experiments were kept for some days under observation after they had been caught. About 13.5 per cent of these (111 Calcutta sparrows) were found to be infected. The healthy ones that remained were divided into two lots. "Both lots were kept at night in their cages in separate mosquito-nets. To one lot infected mosquitoes were introduced, while the other (control lot) were preserved from the bites of the mosquitoes in the laboratory." About

80 per cent of the sparrows exposed to infected mosquitoes subsequently exhibited proteosoma in their blood, while out of a large number (about 40) of control sparrows only one showed infection on a subsequent examination. In this one sparrow very few parasites were present, and Ross believes that they were simply overlooked at the first examination. After some weeks had passed these control sparrows were in turn exposed to the bites of infected mosquitoes and most of them acquired the disease. As already stated only 15 of the 111 sparrows caught exhibited the proteosoma in their blood, but only 2 of the birds showed more than one parasite in a field. On the other hand the birds exposed to the mosquito-inoculations exhibited an enormous number of parasites in their blood. Ross finds that birds which once show proteosoma always continue to show them in roughly the same numbers. He says it is easy to distinguish between a new and an old infection by the almost invariable presence of the larger, discrete pigment containing parasites, these not being found at the onset of an infection caused by mosquito-bites.

Ziemann[301] (1898) states that he fed flies—he does not mention the species—with human blood taken from a case of æstivo-autumnal malaria, with pieces of spleen from a case of pernicious fever, as also with the organs of birds affected with hæmatozoal disease. The flies were examined 4 hours after they had been fed, but no trace of parasites could be found. It would have been more to the purpose if Ziemann had experimented with mosquitoes, there being absolutely no ground for the supposition that flies play a rôle in the spread of malaria.

We now come to the experiments of Grassi[307a&b] (1898, I and II) who approached the matter in a different manner to Ross. Grassi has made extended researches in Italy and Sicily with the object of determining if there exist any species of mosquitoes peculiar to malarial districts. As there are many places where no malaria occurs, but mosquitoes are numerous, it seems probable that this may depend on the fact of these not being the species suited to act as a host for the malaria parasite. We have seen in the preceding pages how very dependent parasites are on specific hosts. By excluding all the species of mosquitoes found in non-malarial districts, as well as in malarial centers, Grassi was able to find *three species which were confined to areas affected by malaria.* One of

these *Anopheles claviger* Fabr. is constantly present, being most frequent in the worst malarial foyers. It is a large species vulgarly called "Zanzarone" or "Moschino," which Ficalbi ("Culicidæ Europee" cited by Grassi) describes as very common in Italy, especially in the flat country where there is much water that is not too unclean ("non troppo sporche"). This species attacks both man and animals. The coincidence of its presence and malaria is very striking in many parts of Lombardy, Venetia, the Maremme, Tuscany and certain localities in the Roman Campagna. Grassi relates several observations made in July-August, 1898, where persons who had been bitten by this species had acquired malaria. In only one spot, a villa near Saronno, were a very few of these "Zanzarone" present. The other two species which were constantly found were *Culex penicillaris* Rondani, which was also numerous, and *Culex malariae* Grassi a new as yet undetermined species. Grassi states that no rôle can be attributed to the genera *Ceratopogon*, *Simulia*, *Aedes*, and *Phlebotomus*, nor to the species *Culex pipiens*, *Culex Richiardii*, *Culex annulatus*, *Culex hortensis*, *Anopheles bifurcatus*, *Anopheles nigripes*, *Culex spathipalpis*, *Culex pulchritarsis* and *Culex elegans*.

Grassi's servant, who acquired malaria, had been bitten a month before by the three species named above. Grassi tried to cause malaria by mosquito-bites whilst at Rovellasca, using *A. claviger* but he had no success, because, as he says, this species does not, as a rule, bite any more in Lombardy during September. He gives data which show that certain mosquitoes bite at different times during the course of the day and night, but most of them bite in the evening at twilight. Grassi observed that the mosquitoes did not bite him; and though he was much exposed for over 30 days in malarious districts he did not acquire malaria. Six boys who accompanied him and aided him in collecting mosquitoes were exposed respectively 12, 7, 4, 4, 2, and 2 days. The first was bitten about 50 times, the others 20, 5, 2, 50, and 0 times respectively by the "Zanzarone," whilst all six were repeatedly bitten by *C. penicillaris*. Only the first boy had a light attack of fever (there was no examination of the blood made) which was checked by the administration of quinine.

He cites an observation where the children of a family who were protected by mosquito-nets remained free from malaria, whilst one child which had been bitten acquired the disease.

Culex malariae was found on the marshes between Ravenna and Cervia; on the Pontine Marshes it was less common than the other two species, whilst it was not encountered in malarial districts in Sicily. As yet only *A. claviger* and *C. penicillaris* have been encountered in Sicily together with *C. Richiardii* (abundant at Lentini).

The following experiment was then carried out by Grassi and Bignami. Mosquitoes, comprising the three species *Culex penicillaris*, *Culex malariae*, and *A. claviger* were collected at Maccarese, a malarial foyer 22 miles from Rome on the Civita Vecchia Road. The insects were brought to Rome where they were allowed to bite a patient (who consented to the experiment) in the Santo Spirito Hospital. The patient, a man who had been an inmate of the hospital for 6 years, had never had malaria. He was confined at night in a room in which vessels containing mosquito larvæ were placed, and a new supply of these was placed in the room every 4 to 6 days. The patient was severely bitten by the mosquitoes which developed from the larvæ. The result was that *the man acquired malaria*, with æstivo-autumnal parasites in his blood. The details of this experiment were published by Bignami[313]. Grassi believed that infection was due to the agency of the first species above named, as it was the most numerous. *A. claviger* was only present in exceedingly small numbers, and perhaps none of this species bit the patient. (It has since been proved that it could only have been *A. claviger* that caused infection.)

Grassi says that he has not succeeded in infecting birds by allowing mosquitoes ("Zanzare") to bite them. He has found that certain districts may be malarial for birds and not for man, and the reverse. Dionisi[312] (1898) believes that the halteridium infection in pigeons is caused by mosquitoes, as the infection occurs as a rule after the birds have moulted and are more liable to be bitten by mosquitoes. The reasons which led Grassi to believe in the mosquito-malaria theory are chiefly the facts which are known in connection with the rôle of ticks in Texas fever, of mosquitoes in Filariasis and fleas in a filarial disease of dogs which we have considered already. He believes that man infects the mosquito and the mosquito again infects man. He believes that in man infection occurs solely through infected mosquitoes. He expresses the same opinion as Ross that malarial patients may be indirectly a source of

danger. He cites four objections which have been brought forward against the mosquito-theory: 1. The great increase of cases after rains; 2. The appearance of malaria in consequence of the turning up of the soil; 3. The development of malaria in places where there are no mosquitoes; 4. The occurrence of cases in parts which have been long left uninhabited. The sudden development of malaria after rains was observed by him in a number of cases including that of his servant. The latter developed malaria 24 hours after being caught in the rain in a malarious district. We know that the period of incubation is really much longer. Grassi's servant had previously been exposed for weeks in a malarial country and had been badly bitten by mosquitoes. This is what has also happened in other cases. In the cases following upon the disturbance of the soil which Grassi investigated, he also found that the period which elapsed before the appearance of fever was too short, infection having taken place at some earlier date. He has often been told by medical men that malaria might occur in places where there are no mosquitoes, but in all cases investigated by him mosquitoes were to be found. The observation made by Dionisi, *that bats harbor parasites which are analogous to the malaria-parasite of man*, is an indication of how the parasite may be maintained in nature in the absence of man. This is most probably the case in malarious countries which are rarely visited by human beings.

Grassi states that Celli, Bignami, Dionisi and Bastianelli are all at present engaged in pursuing these studies.

In a paper entitled "The Malaria Problem in the Light of Epidemiology" by Davidson[309] (1898) the writer inquires how far the mosquito hypothesis can be made to harmonize with certain epidemiological facts; such as the development of malaria in consequence of disturbance of the soil; the invasion of countries and districts previously free from infection; the extinction of malaria in countries where it formerly prevailed; the slow spreading of malarial epidemics, in which, as the disease advances, it dies out in the regions just visited; the occurrence of local epidemics caused by the formation of artificial marshy foci; malaria on ships; the prevalence of malaria in northern latitudes at a season of the year when the temperature is under freezing point and when insect life is in abeyance. We have already considered the question of malaria resulting from soil disturbance. The other questions put by Davidson

I should reply to as follows: The invasion of countries previously free from malaria may be due to the importation of the parasite by man or by mosquitoes. In the first case a suitable species of mosquito may be present in the locality. The latter may be also transported thither by ships, or along the lines of railways or other roads of travel. We also know that mosquitoes at times migrate. The extinction of malaria in countries where it has formerly prevailed may be due to a number of conditions, among which changes in the condition of drainage and moisture of the land, as well as of its vegetation, may be mentioned. It has also been observed with regard to other infectious diseases that they appear and disappear, but the reasons for these changes are manifold and are not always clear. It will probably be established that malaria on ships is due to the presence of infected mosquitoes on board. Roe once (as already cited) observed a dozen different species of mosquitoes on a ship that came from a yellow fever infected port and lay at anchor in New York harbor. The fact that adult mosquitoes hibernate in the cellars of houses (see Appendix) and have been known to be troublesome in winter will probably explain the occasional occurrence of malaria during the cold season.

In a brief communication made on the 28th of November, 1898, to the Accademia dei Lincei, Bastianelli, Bignami and Grassi report that they have succeeded in observing the development of crescentic malarial parasites in the intestinal wall of *Anopheles claviger*. They placed four patients who all had æstivo-autumnal fever in a room with 6 *Culex pipiens*, 1 *Anopheles nigripes* and 4 *Anopheles claviger*. The examination of the insects gave a positive result only in the case of two mosquitoes belonging to the last named species. *They observed developmental changes in these mosquitoes similar to those described by Ross.* After some negative results they also succeeded in observing developmental changes in the hæmatozoa of the owl ("civetta" spec.?) and pigeon in *Anopheles claviger* which had been fed with their blood. Bastianelli, Bignami and Grassi also report that at Lentini (Sicily) in October and November no specimens of *Culex penicillaris* nor of *Culex malariae* could be found, whereas *Anopheles claviger* was very numerous.

It is very gratifying to see the statements and investigations of *Ross* apparently confirmed so soon.

Postscript.

In a paper dated December 22,[1] Grassi, Bignami and Bastianelli describe the result of further investigations on the development of malarial parasites in the "Zanzarone" or *Anopheles claviger* Fabr. They examined (*a*) mosquitoes caught in rooms and cabins where malarial subjects slept, others caught in stables and chicken-houses which had sucked the blood of domestic animals, serving as controls. In a second line of experiments (*b*) the *Anopheles* were examined at stated intervals after they had been permitted to suck the blood of malarial patients in the hospital. The development of the parasites was observable in these mosquitoes, whilst they were absent in those fed on normal human blood.

The *Anopheles* are found in houses, stables and chicken-houses, from about the beginning of October, after which they are only found exceptionally outside. The same observation was made in Lombardy, only that the mosquitoes were found in houses, etc., from the beginning of September. Under these conditions the mosquitoes continue to feed about every two days, whilst the eggs do not develop. A temperature of 30° C. prevailed at the time. Whilst 75 per cent of the mosquitoes caught in houses occupied by malarial subjects proved to contain the parasites, the control insects showed none. Some observations made in the beginning of November at 14-15° C. (outside temperature) indicate that the malarial parasites do not develop within the mosquito at this low temperature, at any rate during the first hours after the mosquitoes had been fed on malarial blood. The development of the parasites in mosquitoes kept at 20-22° C. was not as rapid as at 30°, at which temperature the following observations were made:

The æstivo-autumnal parasites, as stated above, when ingested at the time they have reached the mature crescentic stage, develop into hemosporidia within the mosquito. On the second day they are found encapsuled between the muscle-fibers of the mosquito's intestine and are seen to contain pigment granules which are identical with those of the crescentic parasites. The granules occur in masses at the periphery, or in parallel lines, etc., within the cells. The parasites are vacuolated and very transparent. On the fourth

[1] "Ulteriori ricerche sul ciclo parassiti malarici umani nel corpo del zanzarone." Rendiconti d. R. accad. d. Lincei, Classe di sc. fis. mat. e naturali, 1898. (Reprint 8 pp.)

day the parasites have grown larger and more vacuolated. They contain less pigment and this is irregularly distributed, though it still retains its dark color. After six days the parasites have grown enormously and are seen to project (" facendo hernia ") more than in the last stage, into the insect's body cavity, from which they are separated by the external tunic of the intestine. At this stage the parasites may be readily distinguished with a low power, and, on closer examination, are found to contain innumerable little bodies, refractive droplets presenting the appearance of fat, and less pigment than before. After the seventh day (measure ca. 70 μ.) they contain enormous numbers of filaments arranged in rays about several centers. The filaments measure about 14 μ in length and are very delicate; in some a single, or two, or three, masses of clear homogeneous substance may be distinguished, whilst they are absent in others. If there is any pigment present it is situated in the homogeneous substance. When the capsules are crushed these filaments are seen to issue from them.

The changes here described are similar to those found in other sporozoa. These changes consist in an increase in the volume of the encapsuled protoplasm, and nuclear multiplication which ends (on the 6th day) in the formation of many very minute nuclei surrounded by a small amount of protoplasm (sporoblasts without a capsule) fragments (" nucleus de reliquat ") being left over after the process is completed. The sporoblasts become transformed directly into sporozoites, these being very delicate, filiform with tapered ends and measuring 14 μ in length. After the seventh day ruptured capsules are to be seen still adhering to the intestine, and near them the sporozoites, which, after their escape, become distributed throughout the body cavity, finally accumulating in enormous numbers in the cells or tubules of the salivary glands of the insect. When this has occurred the empty capsules may have disappeared from the intestinal wall, this being apparently due to their being reabsorbed. The sporozoites which occupy the capsules and salivary glands are non-motile, but in one case where they were distributed throughout the body they were seen to move.

The observations made on the development of the tertian parasite within the body of *Anopheles claviger* only extend as yet to the fifth day. These observations are more difficult, because the mature and non-segmenting bodies which are capable of developing

in the mosquito are not as numerous in the blood as are the crescentic parasites of æstivo-autumnal fever. The former parasite differs from the latter in its appearance within the mosquito, the hemosporidia being paler, less refractive, somewhat larger at a corresponding stage of development, besides which they contain less and finer pigment. In mosquitoes which had been repeatedly fed with both kinds of malarial blood, parasites in different stages of development were encountered.

In a few cases, where mosquitoes had been gathered in houses occupied by malarial subjects, as well as in stables, peculiar bodies of varying shape and length were encountered. Some of these bodies were sausage-shaped, were longer than the sporozoites, and exhibited constrictions; others were half as long as the sporozoites and presented an oval, straight or curved appearance. These forms are surrounded by a thick yellowish-brown membrane and contain a body comparable to a sporozoite, this being especially evident in the short forms. Various stages in the development of the membrane have been followed. These bodies are found either encapsuled or lying free in the midst of granular substances. They are evidenly spores, such as are observed in other sporozoa. The further development of these bodies has still to be studied. The striking irregularity of their occurrence suggests the possibility of their being degenerated parasites. Grassi, Bignami and Bastianelli seem to believe that they are resistant spores, which, gaining access to water, may infect the young generation of *Anopheles*, or even more directly, if the latter drink water containing them. The latter view, however, seems improbable. The problem can only be cleared up by further experiment. The possibility that the parasite may pass from the parent mosquito to its young is indicated by the behavior of the Texas fever parasite in ticks. Bignami and Bastianelli think it is difficult to explain certain epidemiological facts without making this assumption; how, for instance, is the appearance of the first cases of æstivo-autumnal fever in the Roman campagna in the end of June or beginning of July to be explained, when cases of infection with the crescentic parasites do not occur? Granting the possibility of their occasional occurrence, this will not explain the regular recurrence of æstivo-autumnal fever at this particular time. As yet all attempts to find the parasite in the mosquito's egg have given negative results, a

fact which indicates that the young mosquito may infect itself with the spores whilst in the larval stage.[1]

In parasites within the cells of the salivary glands of *Anopheles* which were examined after longer periods of time had elapsed since the insects had ingested malarial blood, the following changes were noted (in one case insects which had induced æstivo-autumnal malaria about a month before were examined): At times the whole salivary cell was filled by an agglomeration of rounded or slightly elongated bodies. In others the parasites only occupied the center of the cell; in others, again, there were few or no parasites to be seen. On crushing the gland fusiform bodies escaped from the cells, but they were much shorter and thicker than the sporozoites and exhibited a nucleus. In some cells the ordinary sporozoites could be seen lying alongside the shorter forms. In one case the transformation of the sporozoites into the shorter form was observed through the microscope. Other adjoining cells contained circular, curved or crescentic-looking bodies, sometimes very minute and of a yellowish color. The number of these latter bodies increases with the length of time which elapses subsequent to the infection of the insect. The authors think this indicates that the parasite may degenerate in the salivary gland if it is not expelled within a certain time.

We see from the above that Grassi, Bignami and Bastianelli confirm Ross's observations in every particular. Though his observations were chiefly made on proteosoma-infected birds the results are practically identical. We have seen above that Ross also first observed developmental changes of the crescentic parasites in mosquitoes. Unfortunately for him, the number of his observations was limited. Bastianelli, Bignami and Grassi refer to these observations as follows in a previous paper (4 Dec.):[2] "Il Ross però non avendo seguìto lo svillupo di questi corpi, non poteva con sicurezza riferirli alle semilune, essendo, anche possible che i suoi due mosquitos prima de pungere l'uomo avessero già punto altro animale." They ignore his very clear statement that he used controls.

[1] The Texas fever parasite has also not been found in the eggs of the tick.

[2] See Bibliography.

Note whilst going through the press:—Since the preceding pages were written a number of publications on the subject have appeared. I would refer the reader to a series of reviews regarding them in the Centralblatt für Bakteriologie. I shall from time to time publish such reviews describing the results of the latest researches on malaria.[1]

Some Notes on Mosquitoes.

The term "mosquito," signifying "little fly," has been applied to a large number of insects belonging to the genera *Culex*, *Anopheles*, *Aedes*, *Ceratopogon*, *Simulia* and *Phlebotomus*. These insects are very widely distributed, being found even in the arctic regions. Mosquitoes are also called "gnats" in English, "cousin, maringouin, moustiques" in French, "Stechmücken" in German, "Camari" in Russian, "Zanzari" or "Zanzaroni" in Italy, etc., etc. Riley remarks that they are known to occur in enormous numbers in arctic regions, where a limited number of adult insects are known to *hibernate* during the winter. C. F. Hall (cited by Howard[328], 1896) reported that he encountered them in vast numbers whilst on his expedition in July, 1869. von Nordenskiöld (1883, *loc. cit.*) saw them in great quantities in Greenland. They are very numerous in Lapland (Westermann's Monatsheften, 1876), but according to Count Waldburg they do not occur in Spitzbergen. von Hofmann (cited by Finsch, 1876, *loc. cit.*) suffered greatly from "Mücken" in the Ural mountains. He says he had not seen them more numerous near the Caspian Sea, in the primeval forests on the Yennissei or in tropical regions. Strange to say they are absent on the Island of Waigatsch. von Hofmann saw them appear in the western Urals in June before the ground had begun to thaw. He says (Reisen, p. 183) that they were joyfully greeted as the first messengers of springs, but that in a few days they had lost all sympathy. Finsch who suffered greatly from these pests brought back specimens from the vicinity of the Ob and from the Tundra, which proved to be *Culex pipiens* L. These insects which are called "Camari" by the Russians, disappeared suddenly when the temperature had fallen to 2° (R.?) below zero, and Finsch made

[1] **Nuttall, G. H. F., Neuere Forschungen über die Rolle der Mosquitos bei der Verbreitung der Malaria. Zusammenfassendes Referat. Centralblatt für Bakteriologie, Abtheil. 1, vol. 25, pp. 877-881, 903-911, vol. 26, pp. 140-147, to be continued. (Bibliographies given.)**

observations which led him to conclude that they *hibernated* under the moss which covers the Tundra. Sterling[344] (1891) saw mosquitoes at Mackinaw, Sault Ste. Marie in March, 1844, when the snow, which lay 2 to 4 feet deep on the ground, was being melted by the sun. The insects appeared in thousands and bit his party until sundown. That the adult insects hibernate is well established. Stewart[345] (1891) of North Carolina, saw mosquitoes appear in swarms in March, when several feet of snow lay on the ground. They "literally blackened the banks of snow in sheltered places. These were evidently the insects of the previous summer which were wintering over. The Indians told us that the mosquitoes lived over the winter, and the old ones are the most annoying to them." Westwood[350] (1872 and 1876) saw "common gnats" hibernate in his house at Oxford (England). They had appeared in the house in July and were troublesome during the winter evenings. In April large numbers appeared but these were only females which had hibernated, as he supposed, in a chimney. Wade[347] (1884) saw *Culex ciliatus* Fabricius hibernate in his cellar, and Aaron[314] (1890) made a similar observation. See also Young (Sci. Goss., 1881, cited by Aaron).

Howard[328 329] (1896) says that there are 8 species of mosquito known in the District of Columbia, 4 in New Orleans, 10 on the Island of St. Vincent, whilst von Osten-Sacken enumerates 21 known species in North America.

Descriptions of *Culex pungens* are given by Riley[1] (1896). He found this species multiplied in the spring in small rain-pools which dried up within two weeks. Macloskie[334] (1887-1888) describes the mouthparts and poison apparatus of *Culex taeniorhynchus*. Dimmock[321] (1881) may also be consulted with regard to anatomical details of various diptera. With regard to *Simulium molestum* the "black-fly," see Packard (Am. Nat., II, 589; also quoted in U. S. Dept. Agric., Div. of Entomol., Bulletin 5, n. s., 1896). Descriptions of the development and life-history of these insects will be found in all the larger works on entomology.

I have dwelt on the subject of hibernation because it might be of importance in connection with the study of the malarial parasite in the mosquito. The fact that mosquitoes hibernate would explain the occasional occurrence of malaria in winter.

[1] See U. S. Dept. Agric., Div. of Entomol., Bulletin 5.

Measures Against Mosquitoes.

Drainage of the soil is an effective measure against mosquitoes, as it removes the surface accumulations of water in which these insects breed. Where this cannot be carried out the *rain-holding hollows may*, as Aaron[314] (1890) suggests, *be filled up with earth.* This author (p. 60) also recommends the *flushing of the pools* in which mosquitoes propagate, or in other cases the creation of *active artificial currents*, by means of windmills, which either pump water into the stagnant pools and cause them to overflow, or pump the water out of the pools into a neighboring stream, or on to elevated land which is kept irrigated by the circulating water. Where fish or kerosene cannot be used, the *artificial agitation of the surface of ponds* and water-tanks may be resorted to. Howard[328] (1896) says that this measure has been found practical in San Diego, Texas, where small water-wheels are kept in motion by windmills during the summer. Mosquitoes cannot lay eggs on agitated water, neither can they make their escape from the pupa-case under such conditions without perishing.

Natural enemies. An old remedy against mosquitoes consists in the *introduction of fish into their breeding places.* According to a note in Insect Life, IV, 233, an English gentleman living on the Riviera, was no longer troubled by mosquitoes after he had introduced carp into his water-tanks. Russel[342] (1891) of Bridgeport, Conn., writes that a high tide broke away the dike and flooded the salt meadows at Stratford, Conn. When the tide receded, it left two lakes, nearly side by side, and of the same size. In one a dozen or more fish were left, whilst none were left in the other. After a short time mosquitoes abounded in the latter, whilst about the one containing fish no mosquitoes were to be found. Howard[328] (1896) recommends the introduction into mosquito-breeding ponds in the United States of the common little stickleback (*Gastrosteus aculeatus* or *Pygostens pungitius*) which is very active and voracious. He states that a small fish called "perch" is used for the purpose in Beeville, Texas, and that Urich of Trinidad has also found a little cyprinoid to be very useful there. There are of course many places where mosquitoes breed, where fish could not exist, so the use of fish is naturally restricted. It is interesting in this connection to note that Murray[337] (1885) saw *Culex* destroy very young trout, the adult insect, as Aaron puts it, "literally suck-

ing out their unsuspecting little brains before they could escape." I find that Combes[318] (1896) made a similar observation on the Island of Anticosti. The mosquitoes attacked the "petits poissons filiformes" and sucked out their heads. When released the little fish turned belly upward and floated on the water, dead. These mosquitoes were also seen to attack an allied species of insect while the latter were issuing from the puparium. At this time the young fly is still very soft and is readily sucked out by the other species which attacks it.

The suggestion to use *dragon-flies* and other natural enemies against mosquitoes was made some years ago by Lamborn[332] (1890), who offered prizes for essays on the subject, but there is no chance of this method of mosquito-extermination being practically applied. (See the opinions of Uhler, Aaron, Packard, Beutenmüller, Weeks.) *Spiders*, *bats* and *birds* with nocturnal habits destroy large quantities, but make practically no impression on the number of these insects.

The planting of trees has been found of use in malarial districts. Trees will modify the conditions of drainage in the soil and the character of the vegetation. It is quite possible that in the case of the *Eucalyptus* another factor has to be taken into account. It is very probable that *the smell of this tree drives away mosquitoes.* It is well known that the eucalyptus tree has been especially recommended for planting in malarious regions. Sanders[343] (1893) who had no idea of the mosquito-malaria theory reports an observation which indicates very clearly that this tree repels mosquitoes. He planted *Eucalyptus globulus* about his country house in Fresno County, California, with the result that the mosquitoes disappeared from about the house, whilst they abounded all around in the immediate vicinity. His eucalyptus grove was frequently resorted to by campers for this very reason. Eaton[322] (1893) claims that a branch of eucalyptus placed next to the pillow will keep off mosquitoes, and we have in oil of eucalyptus a well-known remedy against these insects. That the planting of eucalyptus trees is not a "sovereign remedy" may be gathered from the fact that malaria still prevails at Tre Fontane outside of Rome in spite of the eucalyptus plantations.

The *castor oil plant* is also stated to keep off mosquitoes, being planted for that purpose about houses in Egypt (note in Indian

Medical Record, 16 March, 1898). In an editorial note in Janus (Sept. to Oct., 1898, p. 214) it is said that "insects, grasshoppers, earth-worms" and even moles, will not approach the castor oil plant which exerts a decidedly repellent action.

Kerosene. Delboeuf[320] (1895) says that he has used kerosene as a remedy against mosquitoes for fully fifty years, and states that its use is referred to in the Journal Pittoresque for 1847, p. 80, where it is spoken of as something already well known. (Delboeuf very unjustly blames Howard for claiming it as his discovery. It is certain that he would not have done so if he had read Howard's original publications instead of a review.) Howard[326] (1893) says he has known of its being used for upwards of twenty years.

The first *experiments* with kerosene were made by Aaron[314] (1890, p. 63) who found that a drop of petroleum placed on a pool 10 inches square, caused the death of all the mosquito larvæ and pupæ it contained within 15 minutes. The thin layer of oil caused the death of the insects, because they could no longer breathe, consequently it is immaterial if the pool is deep or not. *Crustacea* and *odonata* larvæ which were also present in the pool remained uninjured. Aaron recommends the application of a kerosene film to pools, because it is harmless, effective, easy to use, and cheap. For three dollars enough petroleum may be procured to make five applications in a season to a sheet of water covering 100 acres. It may be sprayed on the water, or allowed to spread of itself. Howard[326] (1893) says he destroyed all the insects in a pool 60 feet square by the use of petroleum, no living insects being seen in it for 10 days after. (This experiment was conducted in the summer of 1892 at his place in the Catskill mountains.) The thin layer of oil had no deterrent effect on the female mosquitoes, but it *destroyed them when they attempted to lay their eggs* on the oiled surface. He estimated that 7400 insects were killed by the oil, the influence of which "outlasted all ocular or odorous evidence of its presence." He calculated that a barrel of oil costing $4.50 will suffice for the treatment of 96,000 square feet of water surface. He advises the use of petroleum *early in the season*, as in this way the mosquitoes are destroyed before a new lot of eggs are laid. Howard[327] reported next year (1894) that he had waged a kerosene war against mosquitoes on an estate near Washington. A pond, having a surface of 4000 square feet, situated near the house, was found to be the

chief source of the mosquitoes. On the 4th of June the pond was covered with a film of the cheapest petroleum (15 gallons) with the result that there were no mosquitoes to be found in it in June and July. Two other small ponds were similarly treated, *the rain-water barrel was closed by a cover*, and two horse troughs were scooped every few days by means of a fine hand net. Smith adds that two similar experiments had been successfully carried out at Long Island. Weed[348] (1895) states that it has been the custom in the French quarter of New Orleans to place kerosene on the water-tanks where mosquitoes are troublesome. He had tried it on water-tanks with good results. Kellogg (cited by Howard[328] 1896) applied kerosene to holes filled with water on the campus at Palo Alto (California) with the same effect. Howard justly remarks that it is absurd to take other precautions when the breeding places for mosquitoes are neglected. We see from the foregoing that we possess a very excellent remedy against mosquitoes in the use of petroleum.

The addition of chemical agents to water has been resorted to with the object of destroying mosquitoes. Prof. R. P. Whitfield (Beutenmüller[315], 1890, p. 123) reports that the people in Atlantic City, N. J., added *copperas* to the water with this object. The addition of *permanganate of potash* (Editorial[323], 1898) has also been suggested. Kawn[331] (1893) says it is a custom in Siam to put a rusty nail in the water jars, it being claimed that this prevents the mosquitoes from breeding in the water. In view of the results obtained with petroleum, chemical agents scarcely need to be further considered.

P. R. Uhler (cited by Lamborn[332], 1890) considers that in certain places on the seacoast the eggs and hibernating female mosquitoes might be effectually exterminated by *burning the grass* over the marshes in the early cold weather of autumn.

Protection of dwellings. Aaron, as also Beutenmüller (1890, *loc. cit.*), recommended the use of *lamp-traps* in the country. Small lamps which surmount a tin-tray containing petroleum are placed on posts or suspended over a pond or marsh at some distance from the dwelling that is to be protected. The mosquitoes are attracted to the light and are destroyed by falling into the petroleum tray beneath. They give figures of such lamps. As stated in the part relating to malaria the use of *smokes, smudges, or fires* in front of

the entrance to houses and tents has been found of use in certain countries. These are extensively used in the Southern States in front of stables to keep off the dreaded Southern Buffalo Gnat (*Simulium pecuarum* Riley). Tin pails with smudges are also hung about the horses' necks as a protection whilst the animals are at work and fires are burnt in the fields so that the smoke they generate is wafted in the direction in which work is being done. Grassi[307a] (1898, I, p. 171) says that mosquitoes cease to bite where there is a current of air, and suggests that an electric *ventilator* might be of use in malarious districts. He adds that there is much to indicate that mosquitoes have a fine sense of hearing, for persons who are speaking are most bitten. The use of *blinds* and *mosquito-nets* is universal in mosquito countries, and it has been found advantageous to darken the rooms. The darkening of stables has been found of use in excluding flies. Osborn[338] believes that the odor of ammonia which accumulates in closed and darkened stables repels mosquitoes.

Where mosquitoes are troublesome in rooms at night, in the absence of mosquito bars, relief may be obtained by *placing a light in an adjacent apartment*, whereby the mosquitoes are attracted away from the person sleeping in the darkened apartment. Riley and Howard[328] (1893) say that *a simple and useful method of catching mosquitoes in houses* has long been used in New Jersey. The shallow tin cover of a box of suitable size is nailed to the end of a stick. A small amount of petroleum is placed in the vessel thus formed and, the stick being held upright, the lid is passed backward and forward near the ceiling. The mosquitoes in attempting to fly away from the ceiling fall into the petroleum and are killed. Campbell[316] (1891) obtained great relief from mosquitoes, black-flies (*Simulium molestum* Harris), and sand-flies during two consecutive seasons of field work in Canada, by *burning pyrethrum* (also known as Persian or Dalmatian powder) in his tent. By so doing he stupefied the flies, which, falling to the floor, could be swept up and destroyed. He says this method is used in the houses and stores of the Hudson Bay Company. A small cone-shaped heap of pyrethrum is placed on a tin and its apex ignited with a match. Howard[328] (1896) advises to prepare the pyrethrum for this purpose by moistening it sufficiently with water to be able to mould it roughly into little cones about the size and shape of a chocolate

drop. These cones are placed on a pan and dried in the oven. If ignited at the apex the cones smoulder slowly. Two to three of them burnt in a room of an evening will give relief by stupefying (not killing) the mosquitoes. Veeder[346] (1880) says that the *leaves of pennyroyal* placed in a room will repel mosquitoes and that the same effect may be obtained if some oil of pennyroyal is allowed to evaporate in the room.

Besides these more general measures *the body may be protected* by *mosquito bars and nets* about the head, *thick gloves* and *clothing which is impenetrable* to the proboscides of the insects. But gloves and veils must frequently be dispensed with. A large number of remedies against mosquitoes have been suggested and tried. *These all consist of applications of odorous substances to the skin the smell of which repels mosquitoes. Oil of pennyroyal* has been very much used for this purpose and is very generally recommended. Weed[348] (1895) states that he has found the application of a small quantity of *kerosene* to the face and hands to be very effective. This remedy deserves further trial. From personal experience on hunting expeditions made in Canada in 1886 and 1887 where a mixture of *oil of tar and sweet-oil* is used to keep off black-flies and mosquitoes, I must say that this remedy affords excellent protection. It would have been impossible to exist without it. As stated by Osborn[338] (1896) the Hudson Bay Company's people use *tar-water* for protection of man and beast against black-flies and other insects. Coal-tar is placed in a shallow vessel and oil of tar or oil of turpentine is added to it and stirred. The vessel is then filled with water and allowed to stand some days until the water is impregnated. The water is used as a wash. Osborn says that animals are best protected against the voracious Southern Buffalo Gnat by greasy, substances, cotton-seed oil alone, or mixed with tar. Fish-oil, or a mixture of kerosene and axle-grease, is also effective. *Unless the substance keeps its odor it is of no use.* Fish-oil (10 gallons) and Ol. animale fœtidum (4 ʒ) is also good, but a continued coating with oily substances weakens the animals. Lembert[333] (1894) of Yosemite, California, writes that the miners in the Minaret Mining District use a mixture of kerosene and mutton tallow on their donkeys, to which it affords immunity from mosquitoes, "while without it their heads become simply a crust of dried blood on the outside, so abundant are the mosquitoes and horse-flies." The use of *oil of*

eucalyptus, oil of peppermint, lemon juice and vinegar have been all recommended as a protection against mosquitoes. Beutenmüller (*loc. cit.*) cites Ross (Ent. Soc., x, 10) as stating that in Simbirsk a strong infusion of the roots of *Triticum repens* is used for this purpose. An infusion of *quassia* has been recommended (Chappell[317], 1880) but its protective properties are denied (Dancer[319], 1880). Horses may be protected by applying mud to their skins. Syrup has also been used. Finsch (1876, *loc. cit.*) found oil of rosemary as also anise-seed oil to be of no use against the attacks of *Culex pipiens* in Siberia. I found quite strongly camphorated vaseline of scarcely any value in Canada. In Janus (Sept.-Oct., 1898, p. 215) the following lotion is recommended against mosquitoes: ℞ Aeth. c. spir. 5 Aq. Coloniensis, Eucalyptoli 10 an. Tinct. pyrethræ 15. This solution to be diluted with 4 to 5 times the quantity of water before it is applied. We have already referred to the use of garlic as a "specific" against malaria. It would be interesting to give sulphur a fair trial.

Pallas (cited by Finsch, 1876, *loc. cit.*) in his travels in Siberia found the only way to drive off mosquitoes was to place a vessel full of smouldering birch-tinder on his back when walking.

Measures Against Flies, Fleas and Bugs.

Besides the measures above given which also serve to keep off blood-sucking insects of various kinds, we may add that house-flies according to common experience are best combated by *cleanliness* in and about the house. Screens placed before the windows, darkening the rooms, and the use of various fly papers and traps may also be resorted to. *Especial attention should be given to stables*, the manure from which should be placed in specially covered pits, or have lime thrown on it. (Howard and Marlatt[830], 1896, etc.) Aaron (1890, *loc. cit.*) recommends spraying compost heaps in which there are fly larvæ and pupæ with petroleum and Beutenmüller states that petroleum sprinkled on stable floors keeps away flies.

Against fleas, the use of benzine, pyrethrum, hot soap-suds, California buhahare have all been recommended and used. Straw mats and carpets favor the establishment of fleas and they accumulate where floors are left unswept, as is often the case when families leave their houses during the summer. Gage (Insect Life, VII, 422) relates an ingenious method of catching fleas in badly infected

rooms. He allowed a servant to whose legs sheets of sticky paper had been tied to walk about the rooms. The fleas which jumped at his legs were caught on the paper. Railliet[242] (1895, p. 806) says a horse blanket will repel fleas by its smell. He found a litter of pine shavings to be useless. He recommends the use of fresh walnut leaves. It is almost superfluous to add that house-dogs should be kept clean.

Against bugs (*Acanthia lectularia* and *Conorhinus sanguisuga*) the use of benzine, kerosene, or a mixture of corrosive sublimate alcohol and turpentine have been recommended. If the bedsteads are of iron, hot water is also effective. (Riley[340, 341], 1889 and 1893; see also U. S. Dept. Agric., Div. Entomol., the Bulletins from 1881 on.) In the Lyon Médical, 10 April, 1898, it is advised to squirt acetic acid into the crevices in beds into which bugs have retreated. It appears that it kills them rapidly. The use of sublimate and water has proved of no avail, but good results have been obtained with camphor, carbolic acid, and coal-oil.

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PLATE I.

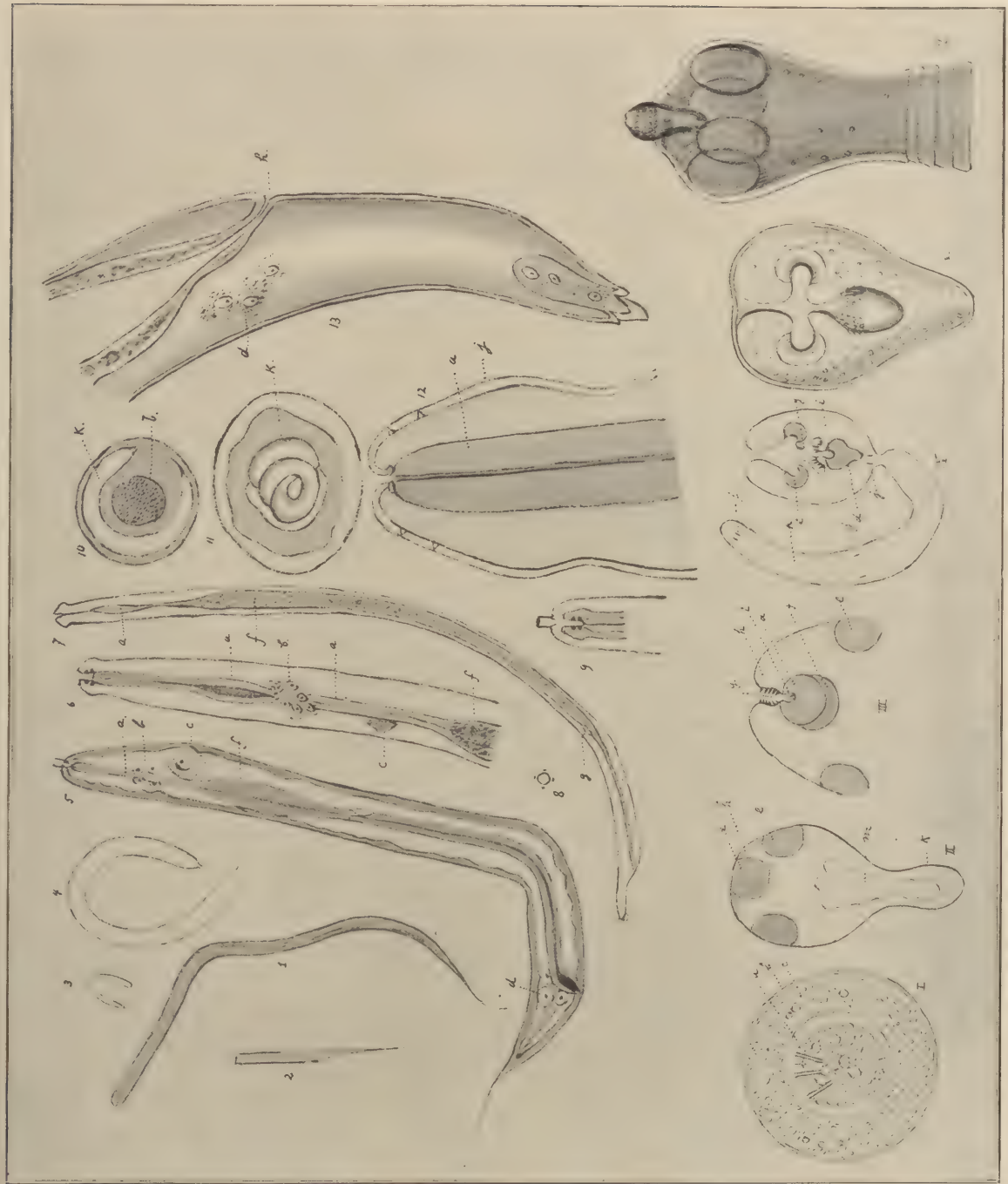
Filaria recondita Grassi.

Metamorphosis of the embryo (Hæmatozoön, Lewis, Grassi) in the dog-flea. After Grassi and Calandruccio 1890.

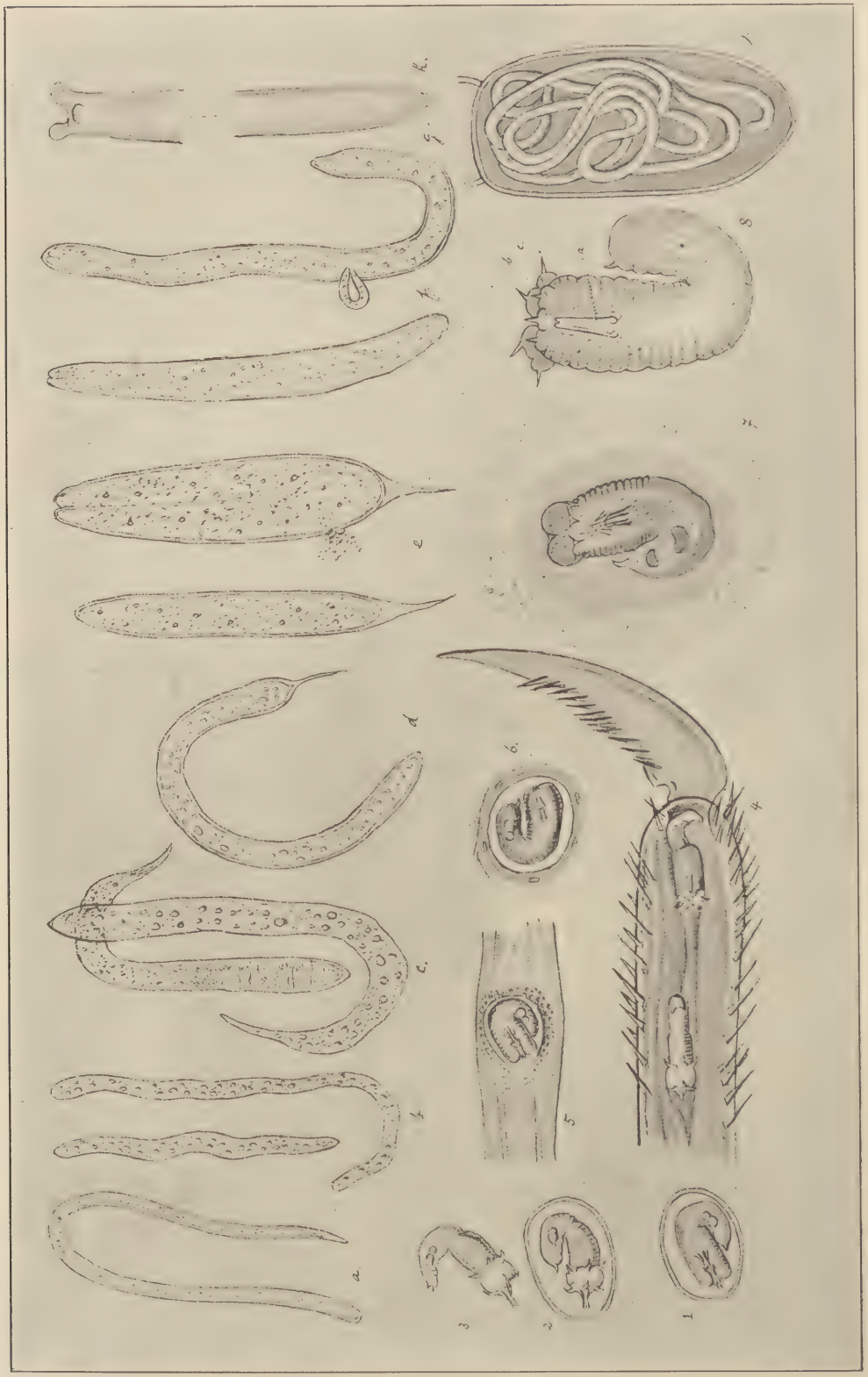
Figs. 1-3. *First stage:* As observed in the blood of the dog and the intestine and body cavity of the flea. The embryo (1) is motile, measures about 280 μ in length by about 5 μ in width, being smaller than that of F. immitis, and is otherwise peculiar through often becoming attached to the cover-glass by its oral extremity, the attached end appearing broad and flattened. The structure is indistinct on account of the very small size of the cells. Anteriorly, a very delicate tubular structure covered with cuticula indicates the esophagus. In embryos which have penetrated the flea's body-cavity traces of an intestine can be seen and the position of the anal orifice conjectured. The surface of the body is covered by a very thin, unstriated, homogeneous cuticula. Fig. 2 represents the manner in which the tail tapers off. Fig. 3, the contour of the young parasite compared with Fig. 4 of the next stage.

Figs. 4-5. *Second stage:* Encountered rarely outside of the fat-cells of the flea. The parasites are mostly motionless and lie curled on themselves. They become shortened almost without broadening, then they broaden almost without shortening, then they grow in both directions and attain their maximal length of 770 μ and breadth of 31 μ. Anteriorly, a finger-shaped papilla apparently filled with clear fluid is formed, and posteriorly the tail runs out to a fine point. A very short pharynx showing cuticular thickenings anteriorly is now visible, the esophagus including a muscular (*a*) and glandular stomach (*f*); the intestine, which is enlarged at the end, always contains (in the embryo) a clear fluid. The body-cavity is easily distinguished. There are indications of a nervous (*b*, *d*) and reproductive system (*g*) and a (?) porous excretorius (*c*).

Figs. 6-9. *Third stage*, which is preceded by moulting and possibly partial histiolysis occurring either in the fat-cells or after the parasite has freed itself. In any case the cuticula of the preceding stages is only thrown off after the embryo leaves the adipose tissue. The worm attains a length of 1.5 mm., the width remaining 31 μ, it exhibits active motion, like an eel. The other changes are indicated in the figures. Fig. 8 represents the mouth with its four papillæ seen from above. Fig. 9, the anterior extremity prior to moulting.



Development of *Filaria recondita* (1-13) and of *Diphyllideum caninum* (I-VI).



Development of *Filaria Bancrofti* (a-h) and *Gordius tolosanus* (1-9).

Figs. 10-13. *Fourth stage:* The worm has grown much thicker and become encysted (Fig. 10 and 11), the sexual organs are more developed and the cuticula thicker. The worm presents in stages 3 and 4 very nearly the adult appearance. In Figs. 10 and 11, (*k*) represents the embryo, and (*l*) the nucleus of the fat-cell.

Metamorphosis of *Diphyllideum caninum.*

I. Completely developed egg: (*a*) the embryo lying within (*b*) the vitelline membrane, and (*c*) the delaminated layer. (After Moniez from Railliet, 1895.)

II–IV. Progressive stages in the development of the larva within the dog-flea. (Schematic. After Grassi and Rovelli 1889). (*d*) Bulbus, (*e*) Sucker, (*f*) developing nervous system, (*g* and *i*) anterior and posterior widenings corresponding to the buccal and pharyngeal cavities of trematodes, (*h*) zona circumbulbaris, (*j*) the six embryonal hooklets in (*k*) the tail, (*m*) primitive body-cavity corresponding according to Grassi to the intestine (Mitteldarm) of trematodes. When the cysticercoid has entered the body of the definite host the tail is dropped off. At the same time that the tail grows, and only a short time before the primitive cavity in the body disappears and the suckers and rostellum have been formed, the anterior part of the body becomes invaginated into the posterior portion (compare III and IV), and we obtain finally the form figured next.

V. Melnikoff's figure of the cysticercoid in Trichodectes (after Leuckart figured in many text-books but inaccurate, through the tail being omitted). This form removed from the insect may be observed to become exvaginated as it would be in the intestine.

VI. Head of the adult tape-worm. The rostrum partially protruded (after Railliet 1895).

PLATE II.

Metamorphosis of *Filaria Bancrofti* Embryos in the Mosquito.

(*a-g.* After Lewis, 1879, drawn to scale, (*h*) after Manson 1884.)

(*a*) Filaria in blood recently ingested by the mosquito, presenting the ordinary appearance, there being no marked change during the first 24 hours (× 300 diam.). On the second day the blood has largely undergone digestion and a few altered filariæ moving about languidly are to be seen. Some of them may actually be dead. Between the 2d and 3d day the stomach may contain no filariæ, and it will then be found that they have wandered into the tissues immediately outside this viscus. It will now be observed (*b*) that some of the filariæ have become considerably thicker, and occasionally specimens will be seen with the tail presenting the appearance (*c*) of a lash, the movements still being very sluggish.

(*d*) More advanced stage (× 300 diam.).

(*e*) Fourth day. Short, thick forms, described as "sausage-shaped" by Manson (× 300 diam.), these being almost perfectly motionless and exhibiting a faint indication of a mouth and alimentary canal, "the escape of a few granules on slight pressure towards the other, usually thicker, end suggests the existence of an anal aperture." Lewis found it difficult to account for the transition of form *c* to form *e*. The form *e* now rapidly increases in size, becomes elongated and presents on the 4th to the 5th day

an appearance midway between *e* and *f*, or like *f* (× 100 diam.), which is thrice as big as *e*.

(*h*) The most highly developed form observed by Manson in a mosquito after 159 hours, measuring $\frac{1}{16}$ by $\frac{1}{825}$ inches, shows the three caudal papillæ. (This figure is upside down.)

(*g*) Represents the highest stage of development observed by Lewis (× 100 diam.), the worm being $\frac{1}{33}$ of an inch in length by $\frac{1}{840}$ wide in the middle. The figure shows the intestine extruded through the worm, which has been ruptured by pressure. Lewis was unable to see anything like sexual differentiation, consequently he could not affirm "that a sojourn in the body of the mosquito and subsequent transference to water suffice to bring the Filaria sanguinis hominis to maturity."

Metamorphosis of *Gordius tolosanus*.

(The figures do not include the free or adult stage. After Meissner, 1855).

1–2. Fully developed embryos within the egg, with retracted and fully projected heads.

3. The same after its escape from the egg.

4. Lowest tarsal joint of an ephemera-larva into which two Gordius-larvæ have bored their way and are migrating towards the trunk.

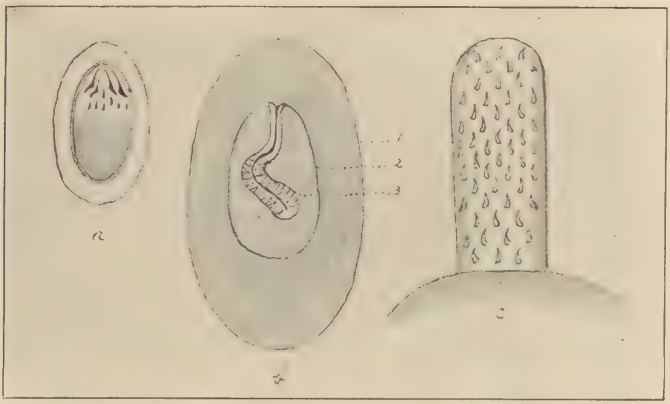
5. Muscle fibers of the insect in and between which the parasites become encysted.

6. Parasite encysted in the insect's body cavity. (After von Linstow, 1893.)

7. First or embryonal larval form of the parasite in *Chloëon dipterum* L. The parasite lies in the adipose tissue and muscles of the insect not encapsuled but surrounded by a clear zone.

8. The same embryo as seen in the egg, (*a*) being the boring apparatus, (*b* and *c*) the two rows of spines.

9. Abdomen of the beetle *Pterostichus niger* from which the dorsal surface has been removed, showing the large Gordius-larva lying curled up within the cavity.



Development of *Gigantorynchus moniliformis.*

PLATE III.

Metamorphosis of *Gigantorynchus moniliformis.*

(After Grassi and Calandruccio, 1888.)

(*a*) Egg 85 by 45 μ in size.

(*b*) Young encysted echinorynchus (measuring with its membranes about 1100 μ in length) in *Blaps mucronata.* (1) outer and (2) inner covering, (3) invaginated proboscis, the hooks being crowded together. They have attained their full size and perhaps also their full numbers.

(*c*) Proboscis 425-450 μ long, with not over 15 rows of hooks.

Echinorynchus moniliformis, Bremser.

(After Grassi and Calandruccio, 1888.)

(*a*) Egg, 85 by 45 μ in size with triple shell. (*b*) Young encysted echinorynchus (about 1100 μ long with membranes) in *Blabs mucronata:* (1) outer, (2) inner membrane, (3) retracted proboscis, the hooks already having attained their full size and perhaps their full number. (*c*) Proboscis 425 by 450 μ long with at most 15 rows of hooklets.